



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (51) International Patent Classification ⁶ : C07D 213/00 | | A2 | (11) International Publication Number: WO 99/02497 |
| | | | (43) International Publication Date: 21 January 1999 (21.01.99) |
| (21) International Application Number: PCT/EP98/04266 (22) International Filing Date: 9 July 1998 (09.07.98) (30) Priority Data: 08/891,691 11 July 1997 (11.07.97) US 08/890,689 11 July 1997 (11.07.97) US (71) Applicant (for all designated States except AT US): NOVAR-TIS AG [CH/CH]; Schwarzwaldallee 215, CH-4058 Basel (CH). (71) Applicant (for AT only): NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT MBH [AT/AT]; Brunner Strasse 59, A-1235 Vienna (AT). (71) Applicant (for all designated States except US): SIBIA NEUROSCIENCES INC. [US/US]; Suite 300, 505 Coast Boulevard South, La Jolla, CA 92037-4641 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): <u>ALLGEIER, Hans</u> [DE/DE]; Lichsenweg 20, D-79541 Lörrach (DE). <u>AUBERSON, Yves</u> [CH/CH]; Kurzellängeweg 7 A, CH-4123 Allschwil (CH). <u>BIOLLAZ, Michel</u> [CH/CH]; Im Kugelfang 31, CH-4102 Binningen (CH). <u>COSFORD,</u> | | Nicholas, David [GB/US]; 7161 Rock Valley Court, San Diego, CA 92122 (US). <u>GASPARINI, Fabrizio</u> [CH/CH]; Weiherhofstrasse 10, CH-4415 Lausen (CH). <u>HECK-ENDORN, Roland</u> [CH/CH]; Blumenweg 20, CH-4144 Arlesheim (CH). <u>JOHNSON, Edwin, Carl</u> [US/US]; 13240 Gunner Drive, San Diego, CA 92129 (US). <u>KUHN, Rainer</u> [DE/DE]; Josef-Pfeffer-Weg 7, D-79540 Lörrach (DE). <u>VARNEY, Mark, Andrew</u> [GB/US]; 13202 Thunderhead Street, San Diego, CA 92129 (US). <u>VELIÇELEBI, Gönül</u> [US/US]; 4688 Tarantella Lane, San Diego, CA 92130 (US). (74) Agent: BECKER, Konrad; Novartis AG, Patent- und Markenabteilung, Lichtstrasse 35, CH-4002 Basel (CH). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published Without international search report and to be republished upon receipt of that report. | |
| (54) Title: PYRIDINE DERIVATIVES | | | |
| <div style="text-align: center;"> <p style="text-align: right;">(I)</p> </div> | | | |
| (57) Abstract | | | |
| Compounds of the formula (I), wherein X and R ₁ to R ₅ are as defined in the description, are useful for treating disorders mediated full or in part by mGluR5. | | | |

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Pyridine derivatives

The invention relates to the use of 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines for modulating the activity of mGluRs and for treating mGluR5 mediated diseases, to pharmaceutical compositions for use in such therapy, as well as to novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines.

It has been found that 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo-pyridines including the pharmaceutically acceptable salts (hereinafter agents of the invention) are useful as modulators of mGluRs. Modulation of mGluRs can be demonstrated in a variety of ways, inter alia, in binding assays and functional assays such as second messenger assays or measurement of changes in intracellular calcium concentrations. For example, measurement of the inositol phosphate turnover in recombinant cell lines expressing hmGluR5a showed, for selected agents of the invention, IC₅₀ values of about 1nM to about 50µM.

In particular, the agents of the invention have valuable pharmacological properties. For example, they exhibit a marked and selective modulating, especially antagonistic, action at human metabotropic glutamate receptors (mGluRs). This can be determined in vitro for example at recombinant human metabotropic glutamate receptors, especially PLC-coupled subtypes thereof such as mGluR5, using different procedures like, for example, measurement of the inhibition of the agonist induced elevation of intracellular Ca²⁺ concentration in accordance with L. P. Daggett et al. Neuropharm. Vol. 34, pages 871-886 (1995), P. J. Flor et al., J. Neurochem. Vol. 67, pages 58-63 (1996) or by determination to what extent the agonist induced elevation of the inositol phosphate turnover is inhibited as described by T. Knoepfel et al. Eur. J. Pharmacol. Vol. 268, pages 389-392 (1994), L. P. Daggett et al., Neuropharm. Vol. 67, pages 58-63 (1996) references cited therein. Isolation and expression of human mGluR subtypes are described in US-Patent No. 5,521,297. Selected agents of the invention showed IC₅₀ values for the inhibition of the quisqualate-induced inositol phosphate turnover, measured in recombinant cells expressing hmGluR5a of about 1nM to about 50µM.

Accordingly the invention relates to agents of the invention for use in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

Disorders associated with irregularities of the glutamatergic signal transmission are for example epilepsy, cerebral ischemias, especially acute ischemias, ischemic diseases of the eye, muscle spasms such as local or general spasticity and, in particular, convulsions or pain.

Nervous system disorders mediated full or in part by mGluR5 are for example acute, traumatic and chronic degenerative processes of the nervous system, such as Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis and multiple sclerosis, psychiatric diseases such as schizophrenia and anxiety, depression and pain.

The invention also relates to the use of agents of the invention, in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by Group I mGluRs.

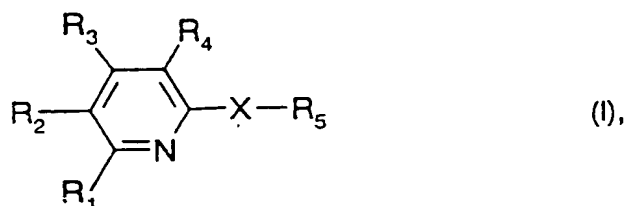
Furthermore the invention relates to the use of agents of the invention for the manufacture of a pharmaceutical composition designed for the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by Group I mGluRs.

In a further aspect the invention relates to a method of treating disorders mediated full or in part by group I mGluRs (preferentially mGluR5) which method comprises administering to a warm-blooded organism in need of such treatment a therapeutically effective amount of an agent of the invention.

In still a further aspect, the invention relates to novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylo- and 2-heteroarylo-pyridines and their salts, and to a process for preparing them.

Moreover the invention relates to a pharmaceutical composition comprising as pharmaceutical active ingredient, together with customary pharmaceutical excipients, a novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylo- or 2-heteroarylo-pyridine or a pharmaceutically acceptable salt thereof.

Agents of the invention are for example compounds of formula I



wherein

R₁ denotes hydrogen, lower alkyl, hydroxy-lower alkyl lower alkyl-amino, piperidino, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower-alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy,

R₂ denotes hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R₃ represents hydrogen, lower alkyl, carboxy, lower alkoxy-carbonyl, lower alkyl-carbamoyl, hydroxy- lower alkyl, di- lower alkyl- aminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R₄ represents hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower-alkoxy or esterified carboxy-lower-alkoxy,

X represents an optionally halo-substituted lower alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms or an azo (-N=N-) group, and

R₅ denotes an aromatic or heteroaromatic group which is unsubstituted or substituted by one or more substituents selected from lower alkyl, halo, halo-lower alkyl, halo-lower alkoxy, lower alkenyl, lower alkynyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylendioxy, lower alkanoyloxy, amino-, lower alkylamino-, lower alkanoylamino- or N-lower alkyl-N-lower alkanoylamino-lower alkoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or

trifluoromethyl-substituted phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, carboxy-lower alkylamino, esterified carboxy-lower alkylamino, amidated carboxy-lower alkylamino, phosphono-lower alkylamino, esterified phosphono-lower alkylamino, nitro, amino, lower alkylamino, di-lower alkylamino, acylamino, N-acyl-N-lower alkylamino, phenylamino, phenyl-lower alkylamino, cycloalkyl-lower alkylamino or heteroaryl-lower alkylamino each of which may be unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted, customary photoaffinity ligands and customary radioactive markers, inclusive of their N-oxides and their pharmaceutically acceptable salts.

Compounds of formula I having basic groups may form acid addition salts, and compounds of the formula I having acidic groups may form salts with bases. Compounds of formula I having basic groups and in addition having at least one acidic group, may also form internal salts.

Also included are both total and partial salts, that is to say salts with 1, 2 or 3, preferably 2, equivalents of base per mole of acid of formula I, or salts with 1, 2 or 3 equivalents, preferably 1 equivalent, of acid per mole of base of formula I.

For the purposes of isolation or purification it is also possible to use pharmaceutically unacceptable salts. Only the pharmaceutically acceptable, non-toxic salts are used therapeutically and they are therefore preferred.

Halo in the present description denotes fluorine, chlorine, bromine or iodine.

When X represents an alkenylene group, configuration trans is preferred.

Preferred compounds of formula I are those wherein

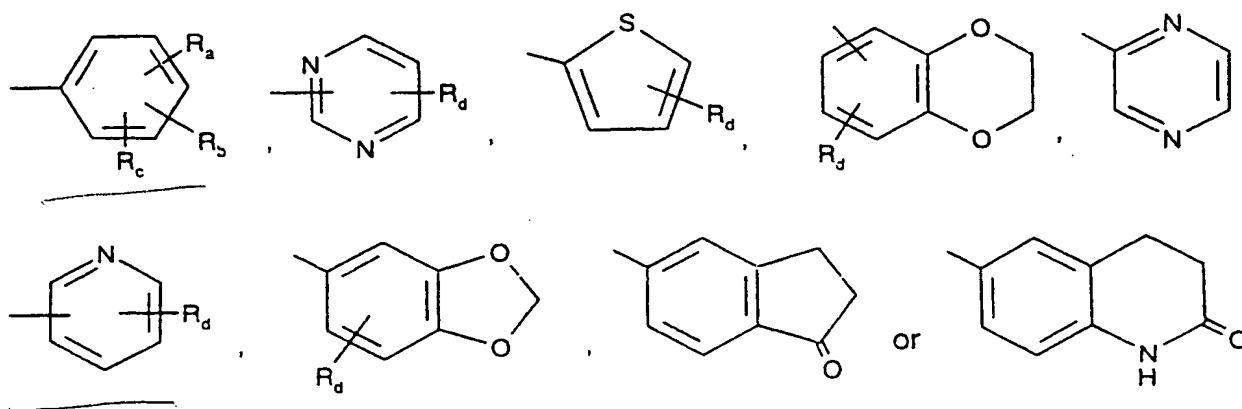
- X represents an optionally halo-substituted (C₂₋₄) alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms,
- R₁ is hydrogen, (C₁₋₄) alkyl, (C₁₋₄) alkoxy, hydroxy(C₁₋₄) alkyl, cyano, ethynyl, carboxy, (C₁₋₄) alkoxycarbonyl, di(C₁₋₄) alkylamino, (C₁₋₆) alkylaminocarbonyl, trifluoromethylphenylaminocarbonyl,
- R₂ is hydrogen, hydroxy, (C₁₋₄) alkyl, hydroxy (C₁₋₄) alkyl, (C₁₋₄) alkoxy, carboxy, (C₂₋₅) alkanoyloxy, (C₁₋₄) alkoxycarbonyl, di(C₁₋₄) alkylamino(C₁₋₄) alkanoyl,

di(C₁₋₄)alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t-butylloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R₃ is hydrogen, (C₁₋₄) alkyl, carboxy, (C₁₋₄)alkoxycarbonyl, (C₁₋₄)alkylcarbonyl, hydroxy(C₁₋₄)alkyl, di(C₁₋₄)alkylaminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R₄ is hydrogen, hydroxy, (C₁₋₄)alkoxy, carboxy, (C₂₋₅)alkanoyloxy, (C₁₋₄)alkoxycarbonyl, amino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkyl, carboxy (C₁₋₄)alkylcarbonyl, (C₁₋₄)alkoxycarbonyl(C₁₋₄)alkoxy, hydroxy(C₁₋₄)alkyl, di(C₁₋₄)alkylamino(C₁₋₄)alkoxy, m-hydroxy-p-azidophenylcarbonylamino(C₁₋₄)alkoxy, and

R₅ is a group of formula



wherein

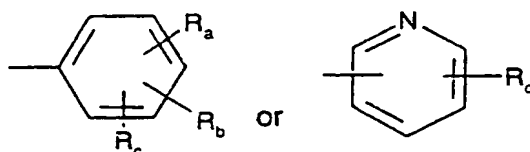
R_a and R_b independently are hydrogen, hydroxy, halogen, nitro, cyano, carboxy, (C₁₋₄)alkyl, (C₁₋₄)alkoxy, hydroxy(C₁₋₄)alkyl, (C₁₋₄)alkoxycarbonyl, (C₂₋₇)alkanoyl, (C₂₋₅)alkanoyloxy, (C₂₋₅)alkanoyloxy(C₁₋₄)alkyl, trifluoromethyl, trifluoromethoxy, trimethylsilylethynyl, (C₂₋₅)alkynyl, amino, azido, amino (C₁₋₄)alkoxy, (C₂₋₅)alkanoylamino(C₁₋₄)alkoxy, (C₁₋₄)alkylamino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino (C₁₋₄)alkoxy, (C₁₋₄)alkylamino, di(C₁₋₄)alkylamino, monohalobenzylamino, thienylmethylamino, thienylcarbonylamino, trifluoromethylphenylaminocarbonyl, tetrazolyl, (C₂₋₅)alkanoylamino, benzylcarbonylamino, (C₁₋₄)alkylaminocarbonylamino, (C₁₋₄)alkoxycarbonyl-aminocarbonylamino or (C₁₋₄)alkylsulfonyl,

R_c is hydrogen, fluorine, chlorine, bromine, hydroxy, (C₁₋₄)alkyl, (C₂₋₅)alkanoyloxy, (C₁₋₄)alkoxy or cyano, and

R_d is hydrogen, halogen or (C₁₋₄)alkyl.

More preferred compounds of formula I are those wherein X is as defined above and

- R_1 is hydrogen, (C_{1-4}) alkyl, (C_{1-4}) alkoxy, cyano, ethynyl or $di(C_{1-4})$ alkylamino,
 R_2 is hydrogen, hydroxy, carboxy, (C_{1-4}) alkoxy carbonyl, $di(C_{1-4})$ alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,
 R_3 is as defined above,
 R_4 is hydrogen, hydroxy, carboxy, (C_{2-5}) alkanoyloxy, (C_{1-4}) alkoxy carbonyl, amino (C_{1-4}) alkoxy, $di(C_{1-4})$ alkylamino (C_{1-4}) alkoxy, $di(C_{1-4})$ alkylamino (C_{1-4}) alkyl or hydroxy (C_{1-4}) alkyl, and
 R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, halogen, nitro, cyano, (C_{1-4}) alkyl, (C_{1-4}) alkoxy, trifluoromethyl, trifluoromethoxy or (C_{2-5}) alkynyl, and R_c and R_d are as defined above.

The agents of the invention include, for example, the compounds described in the examples hereinafter.

The usefulness of the agents of the invention in the treatment of the above-mentioned disorders could be confirmed in a range of standard tests including those indicated below:

At doses of about 10 to 100 mg/kg i.p. or p.o. with pretreatment times of 15 min. to 8 hours, the agents of the invention show anticonvulsive activity in the electroshock induced convulsion model [cf. E.A. Swinyard, J. Pharm. Assoc. Scient. Ed. 38, 201 (1949) and J. Pharmacol. Exptl. Therap. 106, 319 (1952)].

At doses of about 4 to about 40 mg/kg p.o., the agents of the invention show reversal of Freund complete adjuvant (FCA) induced hyperalgesia [cf. J. Donnerer et al., Neuroscience 49, 693-698 (1992) and C.J. Woolf, Neuroscience 62, 327-331 (1994)].

For all the above mentioned indications, the appropriate dosage will of course vary depending upon, for example, the compound employed, the host, the mode of administration and the nature and severity of the condition being treated. However, in general, satisfactory results in animals are indicated to be obtained at a daily dosage of from about 0.5 to about 100 mg/kg animal body weight. In larger mammals, for example humans, an indicated daily dosage is in the range from about 5 to 1500 mg, preferably about 10 to about 1000 mg of the compound conveniently administered in divided doses up to 4 times a day or in sustained release form.

Preferred compounds for the above mentioned indications include (3-{2-[2-trans-(3,5-dichlorophenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethylamine (A), 2-methyl-6-styryl-pyridine (B), 2-(3-fluoro-phenylethynyl)-6-methyl-pyridine (C) and 2-(4-ethoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine (D). It has for example been determined that in the above-mentioned electroshock induced convulsion model, compounds A and B show anticonvulsive activity with ED₅₀s of 30 and 35 mg/kg i.p. respectively (pretreatment times: 4 hours and 15 min. respectively) and that in the above-mentioned FCA induced hyperalgesia model, compounds C and D show reversal of the hyperalgesia with ED₅₀s of 4.2 and 19 mg/kg p.o. respectively (post-treatment time: 3 hours).

As indicated above, the agents of the invention include novel 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-aryloxy- and 2-heteroaryloxy-pyridines and their salts, hereinafter referred to as "compounds of the invention".

Compounds of the invention include compounds of formula I as defined above, and their salts, wherein X and R₁ to R₅ are as defined above, provided that when R₃ is hydrogen, a) in compounds of the formula I in which R₁, R₂ and R₄ are hydrogen, R₅ is different from phenyl, monohalophenyl, 2,4- and 3,4-dichlorophenyl, 3- and 4-trifluoromethylphenyl, methylphenyl, 3,4- and 2,5-dimethylphenyl, 4-isopropylphenyl, 3,5-di-tert.-butylphenyl, methoxyphenyl, 3,4-dimethoxyphenyl, 2,4,5- and 3,4,5-trimethoxyphenyl, hydroxyphenyl, 3,5-dihydroxyphenyl, 4-hydroxy-3,5-dimethyl-phenyl, 3-hydroxy-4-methoxy- and 4-hydroxy-3-methoxy-phenyl, 4-hydroxy-(3-methyl-5-tert.-butyl-, 2- and 4-acetylamino)phenyl, 3,5-diisopropyl- and 3,5-di-tert.-butyl)phenyl, 4-carboxy- and 4-ethoxycarbonylphenyl, 4-cyanophenyl, 3-methoxycarbonylphenyl, 3-carboxy-5-methoxy-phenyl, 2-pyridinyl, 5-chloro-2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene, or R₅ is different from phenyl, 4-methylphenyl, 4-methoxyphenyl, 4-bromophenyl and 2- and 4-chlorophenyl when

X denotes 1,2-propylene attached to R_5 in 2-position, or R_5 is different from phenyl, 2- and 4-chlorophenyl and 3-methoxyphenyl when X denotes 1,2-propylene attached to R_5 in 1-position, or R_5 is different from 4-methoxyphenyl when X denotes 2,3-but-2-enylene or 1,2-but-1-enylene attached to R_5 in 2-position, or R_5 is different from 4-methoxyphenyl and 4-isopropylphenyl when X denotes 2,3-pent-2-enylene attached to R_5 in 3-position, or R_5 is different from phenyl, 4-methylphenyl, methoxyphenyl and 4-hydroxyphenyl when X denotes 3,4-hex-3-enylene;

b) in compounds of the formula I in which R_1 is methyl and R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl, 2-methoxyphenyl, 2-chlorophenyl, 4-cyanophenyl, 2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene;

c) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is carboxy, R_5 is different from phenyl, 3-methylphenyl, 4-methoxyphenyl and 4-bromophenyl when X denotes ethenylene;

d) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is methyl, R_5 is different from phenyl, 3-methoxy-, 4-methoxy- and 3,4-dimethoxyphenyl, 2-chloro- and 2,4-dichlorophenyl and 6-methyl-pyrid-2-yl when X denotes ethenylene or R_5 is different from phenyl when X is 1,2-prop-1-enylene attached to R_5 in 2-position;

e) in compounds of the formula I wherein R_1 and R_2 are hydrogen and R_4 is 2-dimethyl-aminoethoxycarbonyl or 3-dimethylaminopropylloxycarbonyl, R_5 is different from 4-methoxyphenyl when X denotes ethenylene;

f) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is 2-dimethoxyethoxy, R_5 is different from phenyl, 4-methylphenyl and 4-methoxycarbonylphenyl when X denotes ethenylene;

g) R_5 is different from phenyl when R_1 and R_2 are hydrogen and R_4 is hydroxy or ethoxycarbonyl, or when R_1 and R_2 are hydrogen and R_4 is hydroxy, or when R_1 is methyl, R_2 is hydrogen and R_4 is methoxy, or R_1 is but-1-enyl, R_2 is hydrogen and R_4 is hydrogen, or R_1 is hydrogen and R_4 is 2-dimethoxyethoxy, and X is, in each case, ethenylene, and provided that, when R_3 is hydrogen and X is ethynylene,

a') R_5 is different from phenyl, 2- and 4-nitrophenyl, 4-aminophenyl, 4-chlorophenyl, 4-methylphenyl, 4-methoxyphenyl, 4-ethoxycarbonylphenyl, 5-formyl-2-methoxyphenyl, 5-carboxy-2-methoxyphenyl and pyridyl when R_1 , R_2 and R_4 are hydrogen;

b') in compounds of the formula I in which R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl, 6-methylpyridin-2-yl and 2-methoxyphenyl when R_1 is methyl, R_5 is different from 6-bromopyridin-2-yl when R_1 is bromo, and R_5 is different from 6-hexyloxypyridin-2-yl when R_1 denotes hexyloxy;

c') in compounds of the formula I wherein R_1 and R_4 are hydrogen, R_5 is different from phenyl, 4-aminophenyl and 4-propylphenyl when R_2 is methyl, R_5 is different from phenyl, 4-cyanophenyl and 4-pentylphenyl when R_2 is ethyl, R_5 is different from 3-cyano-4-ethoxyphenyl and 3-bromo-4-methoxyphenyl when R_2 is butyl, R_5 is different from 4-methoxyphenyl and 4-butoxyphenyl when R_2 is pentyl, R_5 is different from 4-tert.-butylphenyl, 3-tert.-butyl-4-hydroxyphenyl, 4-tert.-butyl-3-hydroxyphenyl, and 4-hexyloxyphenyl when R_2 is carboxy, R_5 is different from phenyl when R_2 is methoxycarbonyl or methylcarbamoyl, R_4 is different from 3-tert.-butylphenyl, 3-tert.-butyl-4-hydroxyphenyl and 4-(4-methylpentyl)phenyl when R_2 is ethoxycarbonyl, and R_5 is different from 4-pentyloxyphenyl when R_2 is 2-methylbutoxycarbonyl;

d') in compounds of the formula I wherein R_1 and R_2 are hydrogen, R_5 is different from phenyl when R_4 is hydroxy, methyl, ethyl, carboxy, methoxycarbonyl or carbamoyl.

Preferred compounds of the invention are as indicated above for the agents of the invention.

The compounds of the invention can be prepared in analogy to the synthesis of known compounds of formula I.

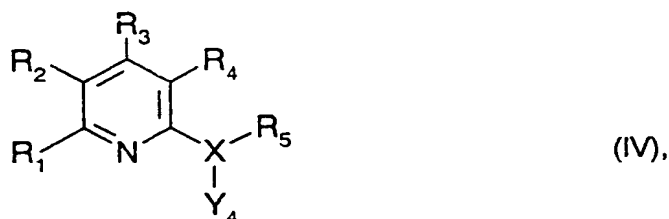
Thus the compounds of the invention which are of formula I can be prepared for example by a process which comprises

a) reacting a compound of the formula II



with a compound of the formula $Y_2 - R_5$ (III), in which either one of Y_1 and Y_2 denotes lower alkanoyl and the other one represents lower alkyl or triarylphosphoranylidene-methyl, or one of Y_1 and Y_2 denotes a reactive esterified hydroxy group and the other one represents a group $Y_3 - X$ in which Y_3 is hydrogen or a metallic group, and R_1 , R_2 , R_3 , R_4 and R_5 have the meanings indicated hereinbefore and functional groups R_1 , R_2 , R_3 and R_4 as well as functional substituents of R_5 may be temporarily protected, or

b) eliminating $H - Y_4$ from a compound of the formula IV



in which Y_4 denotes an electrofugal group and R_1 , R_2 , R_3 , R_4 , X and R_5 have the meanings indicated hereinbefore and functional groups R_1 , R_2 , R_3 and R_4 as well as functional substituents of R_5 may temporarily be protected, removing any temporary protecting groups

and, if desired, converting a compound of formula I obtainable by the above-defined processes into a different compound of formula I, resolving a mixture of isomers that may be obtained into the individual isomers and/or converting a compound of formula I having at least one salt-forming group obtainable by the above-defined processes into a salt, or converting a salt obtainable by the above-defined processes into the corresponding free compound or into a different salt.

A lower alkanoyl Y_2 or, more preferably, Y_1 group is, for example, a C_1 - C_3 alkanoyl group, such as formyl, acetyl or propionyl, especially formyl. A lower alkyl group Y_1 or, more preferably, Y_2 is, for example, a C_1 - C_3 alkyl group, such as methyl, ethyl or propyl, especially methyl. Triarylphosphoranylidene-methyl Y_2 or, more preferably, Y_1 is, for example, triphenylphosphoranylidene-methyl.

When one of Y_1 and Y_2 denotes a reactive esterified hydroxy group and the other one represents a group of the formula Y_3-X in which Y_3 denotes hydrogen, the condensation is preferably performed according to the Heck coupling method, for example, in the presence of copper or of a copper catalyst or of a noble metal/phosphine catalyst, such as Palladium or a PdII salt in the presence of triaryl phosphine, for example, Palladium acetate, and of triphenylphosphine, or in the presence of bis-triphenylphosphine-palladium dichloride, preferably in the presence of a tri-lower alkyl amine, for example, trimethylamine, advantageously in the presence of Cu^I-I , in a polar organic solvent such as N,N-di-lower alkyl-alkanoic acid amide, for example, dimethylformamide, a di-lower alkyl sulfoxide, for example, dimethylsulfoxide, or dioxan, at temperatures from appropriately $15^\circ C$ to appropriately $120^\circ C$, preferably at the boil.

When one of Y_1 and Y_2 denotes a reactive esterified hydroxy group and the other one represents a group of the formula Y_3-X in which Y_3 denotes a metallic group such as a

halo-magnesium group, the reaction is preferably performed according to Grignard method, wherein the metallic intermediate is preferably formed *in situ*.

When one of Y_1 and Y_2 denotes lower alkanoyl and the other one represents lower alkyl, the intermolecular condensation of compounds of the formulae II and III is preferably performed according to the Shaw and Wagstaff method or one of its many modifications.

When one of Y_1 and Y_2 denotes lower alkanoyl and the other one represents triarylphosphoranylidene, the condensation is preferably performed according to the well known Wittig olefin-building method, preferably by forming the phosphoranylidene component from a corresponding triarylphosphonium halide *in situ*, for example, by reacting the latter with a metal base, such as an alkali metal hydride, such as sodium hydride, or with a metal-organic base, such as a lower alkyl metal compound, such as butyllithium, or with an alkali metal alkanolate, for example, potassium tertiary butoxide, preferably in an inert organic solvent, such as an aromatic or arylaliphatic hydrocarbon, for example, benzene or toluene, at appropriately -10°C to appropriately 39°C , preferably first at 0° to 10°C and then at ambient temperature.

Electrofugal groups Y_4 are, for example, esterified hydroxy groups, such as hydroxy groups esterified with an organic acid, for example, lower alkanoyloxy or hydroxy groups esterified with an inorganic acid, for example, halo groups, or tertiary amino groups, such as tri-lower alkylamino groups, for example, trimethylamino, or lower-alkyleneamino, lower azaalkyleneamino, lower-oxyalkyleneamino or lower thiaalkyleneamino groups, such as pyrrolidino, piperidino, morpholino or thiomorpholino, or corresponding quaternary ammonium groups.

The protection of functional groups by such protecting groups, the protecting groups themselves and the reactions for their removal are described, for example, in standard works.

The elimination of $\text{H}-Y_4$ from compounds of formula IV can be performed in a customary manner. Thus, water or lower alkanoyl acids may be eliminated by means of azeotropic distillation, for example, in toluene, advantageously under mild-acidic conditions. Hydrogen halides may be removed under basic conditions such as reaction with an alkali metal alkanolate, preferably in the corresponding lower alcohol as a solvent or co-solvent, or by heating in the presence of a tertiary amine, such as a tri-lower alkylamine.

The starting materials for the above described reactions are generally known. Novel starting materials can be obtained in manner analogous to the methods for the preparation of known starting materials.

Compounds of formula I obtainable in accordance with the process can be converted into different compounds of formula I in customary manner, for example a free carboxy group may be esterified or amidated, an esterified or amidated carboxy group may be converted into a free carboxy group, an esterified carboxy group can be converted into an unsubstituted or substituted carbamoyl group, a free amino group can be acylated or alkylated, and a free hydroxy can be acylated.

Also, compounds of the formula I can be oxidized by customary methods such as reaction with an organic peroxy acid, yielding the corresponding pyridine-N-oxide derivatives.

Salts of compounds of formula I can also be converted in a manner known *per se* into the free compounds, for example by treatment with a base or with an acid.

Resulting salts can be converted into different salts in a manner known *per se*.

The compounds of formula I, including their salts, may also be obtained in the form of hydrates or may include the solvent used for crystallization.

As a result of the close relationship between the novel compounds in free form and in the form of their salts, hereinbefore and hereinafter any reference to the free compounds and their salts is to be understood as including the free compounds, as well as the corresponding salts.

In a compound of formula I the configuration at individual chirality centers can be selectively reversed. For example, the configuration of asymmetric carbon atoms that carry nucleophilic substituents, such as amino or hydroxy, can be reversed by second order nucleophilic substitution, optionally after conversion of the bonded nucleophilic substituent into a suitable nucleofugal leaving group and reaction with a reagent introducing the original substituent, or the configuration at carbon atoms having hydroxy groups can be reversed by oxidation and reduction, analogously to European Patent Application EP-A-0 236 734.

The invention relates also to pharmaceutical compositions comprising compounds of formula I.

The pharmacologically acceptable compounds of the present invention may be used, for example, in the preparation of pharmaceutical compositions that comprise an effective amount of the active ingredient together or in a mixture with a significant amount of inorganic or organic, solid or liquid, pharmaceutically acceptable carriers.

The pharmaceutical compositions according to the invention are compositions for enteral, such as nasal, rectal or oral, or parenteral, such as intramuscular or intravenous, administration to warm-blooded animals (human beings and animals) that comprise an effective dose of the pharmacological active ingredient alone or together with a significant amount of a pharmaceutically acceptable carrier. The dose of the active ingredient depends on the species of warm-blooded animal, body weight, age and individual condition, individual pharmacokinetic data, the disease to be treated and the mode of administration.

The pharmaceutical compositions comprise from approximately 1% to approximately 95%, preferably from approximately 20% to approximately 90%, active ingredient. Pharmaceutical compositions according to the invention may be, for example, in unit dose form, such as in the form of ampoules, vials, suppositories, dragées, tablets or capsules.

The pharmaceutical compositions of the present invention are prepared in a manner known *per se*, for example by means of conventional dissolving, lyophilizing, mixing, granulating or confectioning processes.

The doses to be administered to warm-blooded animals, for example human beings, of, for example, approximately 70 kg body weight, especially the doses effective in disorders caused by or associated with irregularities of the glutamatergic signal transmission, are from approximately 3 mg to approximately 3 g, preferably from approximately 10 mg to approximately 1 g, for example approximately from 20 mg to 500 mg, per person per day, divided preferably into 1 to 4 single doses which may, for example, be of the same size. Usually, children receive about half of the adult dose. The dose necessary for each individual can be monitored, for example by measuring the serum concentration of the active ingredient, and adjusted to an optimum level.

The following non-limiting Examples serve to illustrate the invention; temperatures are given in degrees Celsius, pressures in mbar.

EXAMPLE 1

3-[2-(6-Methylpyridin-2-yl)-vinyl]-benzonitrile

A solution of 2,6-dimethyl pyridine (4.2ml, 36.28 mMol), 3-cyanobenzaldehyde (4.95g, 37.74 mMol) in acetic anhydride (6.85 ml) is heated under reflux for 16 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 400g). The column is first eluted with toluene (400 ml) and then with toluene/ethyl acetate 95:5. The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/hexane and 3.18 g of white crystals are isolated. (melting point: 91-92°).

EXAMPLE 2:

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile

A solution of 2,6-dimethyl pyridine (5.8 ml, 50 mMol), 2-cyanobenzaldehyde (6.81 g, 52 mMol) in acetic anhydride (9.5 ml) is heated under reflux for 16 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 400g). The column is first eluted with toluene (400 ml) and then with toluene/ethyl acetate 95:5. The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/diisopropyl ether and white crystals are isolated. (melting point: 113-114°).

EXAMPLE 3

2-Methyl-6-[2-(pyridin-4-yl)-vinyl]-pyridine

A solution of 2,6-dimethyl pyridine (5.8 ml, 50 mMol), pyridine-4-carbaldehyde (4.9 ml, 52 mMol) in acetic anhydride (9.5 ml) is heated under reflux for 16 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 900g). The column is first eluted with toluene/acetone 4:1 (5 L), then with toluene/acetone 3:1 (5 L) and finally with toluene/acetone 2:1 (15 L). The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/diisopropyl ether and 0.956 g of white crystals are isolated. (melting point: 72-73°C).

EXAMPLE 4

2-Methyl-6-[2-(pyridin-3-yl)-vinyl]-pyridine

A solution of 2,6-dimethyl pyridine (5.8 ml, 50 mMol), pyridine-3-carbaldehyde (4.9 ml, 52 mMol) in acetic anhydride (9.5 ml) is heated under reflux for 10 hours. The acetic anhydride is then evaporated in vacuo and the residue purified on column chromatography anhydride is then evaporated in vacuo and the residue purified on column chromatography (silica gel 900g). The column is first eluted with toluene/acetone 9:1 (7 L), then with toluene/acetone 4:1 (5 L) and finally with toluene/acetone 2:1 (5 L). The fractions containing the desired compound are combined, evaporated in vacuo. The solid residue is recrystallized from methylene chloride/diisopropyl ether and 4.28 g of a colorless oil which solidify upon standing at 6-8°C.

EXAMPLE 5

2-[2-(3-Bromophenyl)ethynyl]-6-methyl-pyridine

1.2 g (2.8 mMol) of 2-[1,2-dibromo-2-(3-bromophenyl)-ethyl]-6-methyl-pyridine are dissolved in 10 ml of ethanol. 0.9 g (16.1 mMol) of potassium hydroxide (powder) are added, and the resulting suspension is heated under reflux for 4 hours. The suspension is then cooled to room temperature, poured into 100 ml of brine and extracted thrice with 30 ml each of *t*-butyl methyl ether. The combined organic phases are washed with 30 ml of brine, dried over Sodium sulfate, filtrated and evaporated *in vacuo*. 0.720 g of the title compound are obtained as a colorless oil crystallizing on standing; melting point 60-61°.

The starting material can be obtained as follows:

a) 2-[2-(3-Bromophenyl)-vinyl]-6-methyl-pyridine

A solution of 24 ml (200 mMol) of 2,6-dimethyl pyridine and 25.6 ml (207 mMol) of 3-bromobenzaldehyde in 38 ml of acetic anhydride is heated under reflux for 7.5 hours. The acetic anhydride is then evaporated *in vacuo*, and the residue is dissolved in 500 ml of 4N hydrochloric acid and twice extracted with 200 ml each of hexane. The water phase is then extracted four times with 300 ml each of *tert*.-butyl methyl ether. The combined organic phases are washed twice with 300 ml each of a saturated solution of NaHCO₃ in water, then once with 300 ml of brine (300 ml), dried over sodium sulfate, filtrated and evaporated *in vacuo* yielding 4.2 g of the title compound as colorless crystals of melting point 58-59°.

b) 2-[1,2-dibromo-2-(3-bromophenyl)-ethyl]-6-methyl-pyridine

1 g (3.6 mMol) of 2-(3-Bromo-phenylethynyl)-6-methyl-pyridine are dissolved in 5 ml of carbon tetrachloride, and the solution is heated to 55-60°. A solution of 0.23 ml (4.4 mMol) of bromine Br₂ in 1 ml of carbon tetrachloride is added dropwise. The reaction mixture is maintained at 55-60° for 30 minutes and then cooled to room temperature. The resulting precipitate is collected by filtration and dried *in vacuo*. 1.3 g of the title compound in form of yellow crystals of melting point 164-166° are isolated.

EXAMPLE 6

3-[2-(6-Methylpyridin-2-yl)ethynyl]-benzonitrile

A mixture of 1 g (8.54 mMol) 2-ethynyl-6-methyl-pyridine (prepared in analogy to D. E. Ames et al., Synthesis, 1981, p. 364-5), 2.3 g (12.8 mMol) 3-bromo-benzonitrile, 0.47 g (0.7 mMol) bis-(triphenylphosphine)-palladium-II-chloride, 80 mg (0.41 mMol) cuprous iodide and 1.53 ml (15 mMol) triethylamine in 10 ml dimethylformamide is stirred for 3 hours at 90° C. The reaction mixture is cooled to ambient temperature, poured into water and extracted with dichloromethane. The organic layer is dried over sodium sulfate, filtered, evaporated to dryness and the residue is purified by chromatography on silica gel with hexane/ethyl acetate (4:1) as eluant. Crystallization from hexane of the obtained product affords 0.53 g (28.4 %) of the title compound as brown crystals, melting point 120-3° C.

EXAMPLE 7

In analogous manner to Example 1 (when X is alkenylene) or Example 5 (when X is alkynylene), the following compounds of formula I can be prepared:

| Compound of formula I | Melting point (°C) |
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| 2-Styryl-pyridin-3-ol | 249-252 |
| 2-Methyl-6-[2-(3-nitro-phenyl)-vinyl]-pyridine | 100-101 |
| 2-[2-(2-Chloro-phenyl)-vinyl]-pyridine | colorless oil |
| 2-Methyl-6-styryl-pyridine | 40-42 |
| Acetic acid 6-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester | 75-77 |
| 6-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol | 168-171 |
| Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester | 99-102 |

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| 2-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol | 232-234 |
| 6-Methyl-2-styryl-pyridin-3-ol | 261 dec |
| Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester | 92-94 |
| 2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol | 232-234 |
| (Z)-6-Methyl-2-styryl-pyridin-3-ol | 145-148 |
| 2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridine | 51-52 |
| 2-[2-(2-Fluoro-phenyl)-vinyl]-pyridine | 69-70 |
| 2-[2-(2-Nitro-phenyl)-vinyl]-pyridine | 97-99 |
| Acetic acid 2-[2-(4-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester | 102-103 |
| Acetic acid 6-[2-(4-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester | 130-131 |
| 2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol | 275-278 dec |
| 6-[2-(4-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol | 265-270 dec |
| Acetic acid 6-methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester | 139-140 |
| 6-Methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol | 190-195 dec |
| Acetic acid 2-methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester | 99-100 |
| 2-Methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol | 230-233 dec |
| Acetic acid 2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester | 97-99 |
| Acetic acid 6-[2-(3-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester | 112-114 |
| 2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol | 232-235 |
| 6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol | 230-232 |
| (Z)-(6-Styryl-pyridin-2-yl)-methanol | 69-70 |
| (E)-(6-Styryl-pyridin-2-yl)-methanol | 58-60 |
| 2,2'-(1,2-Ethenediyl)bis[6-methyl]-pyridine | 109-110 |
| Dimethyl-[3-(6-methyl-2-styryl-pyridin-3-yloxy)-propyl]-amine;hydrochloride salt | 136-139 |
| (E)-6-[2-(2-Pyridyl)vinyl]-2-picoline | 56-57 |
| 2-Methyl-6-styryl-pyridine 1-oxide | 102-103 |
| 2-Styryl-pyridine 1-oxide | 156-159 |
| (E)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol | 240-242 |
| (Z)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol; HCl salt | 225-228 |
| 6-Styryl-pyridine-2-carbonitrile | 92-93 |
| 2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridine | light yell. oil |
| 3-Methoxy-6-methyl-2-styryl-pyridine | light yell. oil |
| 6-Styryl-pyridine-2-carboxylic acid amide | 141-142 |
| 2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile | 113-114 |

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| 3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile | 91-92 |
| 4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile | 131-132 |
| 6-Styryl-pyridine-2-carboxylic acid; HCl Salt | 209-212 |
| 6-Styryl-pyridine-2-carboxylic acid methyl ester | 87-88 |
| Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | colorless oil |
| 2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol | 227-229 |
| Acetic acid 2-methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | 102-103 |
| 2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridine | 59-61 |
| 2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridine | 83-85 |
| 2-[2-(2-Chloro-phenyl)-vinyl]-5-ethyl-pyridine | 34-35 |
| 1-(6-Styryl-pyridin-2-yl)-ethanone | 67-68 |
| 6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid ethyl ester | 80-82 |
| 2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid ethyl ester | 70-72 |
| 2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid; HCl salt | 218-219 |
| 3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid | 150-151 |
| 4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid | 206-207 |
| 3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester; HCl salt | 237-238 |
| 4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester | 112-113 |
| 2-Methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 118-119 |
| {3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-methanol; HCl salt | 230-231 |
| 6-Styryl-pyridine-2-carboxylic acid .tert.-butylamide | 87-88 |
| 2-(2-Bromo-2-phenyl-vinyl)-6-methyl-pyridine; HCl salt | 150-154 |
| 2-Methyl-6-phenylethynyl-pyridine; HCl salt | 146-148 |
| 6-Styryl-pyridine-2-carboxylic acid hexylamide; HCl salt | 118-125 |
| 6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid | 219-221 dec |
| 2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid | 168-170 |
| 2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridine | 75-77 |
| 2-Methyl-6-[2-(3-trifluoromethyl-phenyl)-vinyl]-pyridine | 44-45 |
| (E)-6-[2-(4-pyridyl)vinyl]-2-Picoline | 72-73 |
| N,N-Diethyl-3-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide; HCl salt | 227-228 |
| N,N-Diethyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide; HCl salt | 183-184 |
| (E)-6-[2-(3-pyridyl)vinyl]-2-Picoline | yellowish oil |
| {2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid ethyl ester | colorless gum |

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| 3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide; HCl salt | 249-251 |
| 4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide | 160-161 |
| 2-[2-(3-Nitro-phenyl)-vinyl]-pyridine | 127-128 |
| 6-Styryl-pyridine-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide | 126-129 |
| 2-(6-Styryl-pyridin-2-yl)-propan-2-ol, HCl salt | 171-174 |
| 2-Methyl-6-(2-thiophen-2-yl-vinyl)-pyridine, HCl salt | 208-211 |
| 2-[2-(3-Chloro-phenyl)-vinyl]-pyridine | 51-53 |
| 2-[2-(3-Cyano-phenyl)-vinyl]-pyridine | 85-86 |
| 2-[2-(3-Bromo-phenyl)-vinyl]-6-methyl-pyridine | 58-59 |
| 2-[2-(3-Bromo-phenyl)-2-fluoro-vinyl]-6-methyl-pyridine | 58-59 |
| 2-[2-(3,5-Dimethylphenyl)-2-fluoro-vinyl]-6-methyl-pyridine | 70-72 |
| 2-[2-(2,3-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine | colorless oil |
| 2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridine | 67-68 |
| 2-[2-(3-Chloro-phenyl)-1-methyl-vinyl]-pyridine | colorless oil |
| {2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-methanol | 87-90 |
| 2-Methyl-6-[2-(3-trimethylsilanylethynyl-phenyl)-vinyl]-pyridine | yellowish oil |
| 2-[2-(3,4-Difluoro-phenyl)-vinyl]-6-methyl-pyridine | 61-62 |
| 2-[2-(3-Ethynyl-phenyl)-vinyl]-6-methyl-pyridine | yellowish oil |
| 2-[2-(3,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine | yellowish oil |
| 2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridine | yellowish oil |
| 2-[2-(3-Methoxy-phenyl)-vinyl]-6-methyl-pyridine | yellowish oil |
| 2-Methyl-6-[2-(3-phenoxy-phenyl)-vinyl]-pyridine | yellowish oil |
| 2-[2-(3-Benzoyloxy-phenyl)-vinyl]-6-methyl-pyridine | 68-69 |
| 2-[2-(2,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine | 44-45 |
| {2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid | 230-233 |
| (3-[2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy]-propyl)-dimethyl- amine | 203-205 |
| {6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-methanol | 131-133 |
| 2-(3-Bromo-phenylethynyl)-6-methyl-pyridine | 61-63 |
| 2-Methyl-6-{2-[3-(3-trifluoromethyl-phenoxy)-phenyl]-vinyl}-pyridine | yellowish oil |
| 2-[2-(3,5-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine | 43-45 |
| 2-[2-(3-Chloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine | 52-53 |
| Acetic acid 4-bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | yellowish oil |
| Acetic acid 3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | yellowish oil |

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| 2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridine | 73-75 |
| 4-Bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 246-248 |
| Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester | 156-158 |
| Acetic acid 6-[2-(3,5-dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester | 159-161 |
| Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-pyridin-3-yl ester | 154-156 |
| 2-Methyl-6-(2-naphthalen-1-yl-vinyl)-pyridine | yellowish oil |
| 2-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-vinyl]-6-methyl-pyridine | 99-101 |
| 2-Methyl-6-(2-naphthalen-2-yl-vinyl)-pyridine | 97-99 |
| 2-Methyl-6-(2-m-tolyl-vinyl)-pyridine | yellowish oil |
| 2-[2-[3-(3,5-Dichloro-phenoxy)-phenyl]-vinyl]-6-methyl-pyridine | yellowish gum |
| 2-[2-(3-Chloro-phenyl)-propenyl]-6-methyl-pyridine | yellowish oil |
| 2-[2-(2,3-Dihydro-benzofuran-5-yl)-vinyl]-6-methyl-pyridine | 28-90 |
| 2-[2-(4-Fluoro-phenyl)-vinyl]-6-methyl-pyridine | 50-51 |
| 2-Methyl-6-(2-o-tolyl-vinyl)-pyridine | yellowish oil |
| 2-Methyl-6-(2-p-tolyl-vinyl)-pyridine | 85-86 |
| 2-Methyl-6-(2-p-tolyl-propenyl)-pyridine | yellowish oil |
| 3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine | 126-129 |
| (2,3-Dimethoxy-7-nitro-quinoxalin-5-ylmethyl)-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine | pale orange foam |
| N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide | 147 |
| N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide | 156 |
| 2,2-Dimethyl-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-propionamide | 166-168 |
| Thiophene-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide | 197 dec |
| Cyclohexanecarboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide | 215 |
| 1-(4-Bromo-phenyl)-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea | 197 dec |
| 2-Methyl-6-[2-(4-nitro-phenyl)-vinyl]-pyridine | 134-135 |
| 4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine | 147-148 |
| 2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol | 218-220 |
| 6-[2-(3,5-Dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol | 286 dec |
| 2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-ol | 240-242 |
| 2-[2-(6-Chloro-benzo[1,3]dioxol-5-yl)-vinyl]-6-methyl-pyridine | 131-132 |
| 2-[2-(2,3-Difluoro-phenyl)-vinyl]-6-methyl-pyridine | 55-56 |
| 2-[2-(3,4-Dichloro-phenyl)-propenyl]-6-methyl-pyridine | yellowish oil |

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| 2-[2-(3,5-Bis-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine | 85-86 |
| Acetic acid 2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | yellowish oil |
| 2-Methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 118-120 |
| 2-Methyl-6-[2-(2,3,6-trifluoro-phenyl)-vinyl]-pyridine | 59-62 |
| 2-[2-(4-Fluoro-3-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine | yellowish oil |
| 2-Methyl-6-(2,3,6-trifluoro-phenylethynyl)-pyridine | 93-94 |
| Acetic acid 4-chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | yellowish oil |
| Acetic acid 2,6-di-tert.-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | 127-129 |
| 3-(6-Methyl-pyridin-2-ylethynyl)-benzamide | 187-189 |
| Acetic acid 4-bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester | 151-153 |
| 2-(6-Chloro-benzo[1,3]dioxol-5-ylethynyl)-6-methyl-pyridine | 105-106 light brown crystals |
| 2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine | 127-129 |
| 2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-pyridine | 111-113 |
| 5-Azido-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 143 dec |
| 2-[2-(Pyridin-3-yl)ethynyl]-6-methyl-pyridine | light yellow crystals 60-61 |
| N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid | 212-213 |
| 1-tert.-Butyl-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea | 191-192 |
| 5-({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino}-methyl)-7-nitro-1,4-dihydro-quinoxaline-2,3-dione | 250 dec |
| Tetrahydro-furan-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide | 160-161 |
| (1-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-2-phenyl-ethyl)-carbamic acid tert.-butyl ester | colorless foam |
| ((3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl)-methyl)-carbamic acid tert.-butyl ester | colorless foam |
| Diethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine | 217 dec |
| Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine | 225 dec |
| Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine | 183 dec |
| 2-(2-Ethoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine | yellowish oil |
| 2-(3,5-Difluoro-phenylethynyl)-6-methyl-pyridine | yellowish oil |
| 2-(3-Fluoro-phenylethynyl)-6-methyl-pyridine | 26-28 |
| 2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridine | 56-57 |

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| 2-[2-(3,4-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine | 55-56 |
| 2-(3,4-Dichloro-phenylethynyl)-6-methyl-pyridine | 73-74 |
| 2-(4-Ethoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine | 61-62 |
| 2-(4-Fluoro-phenylethynyl)-6-methyl-pyridine | 98-100 |
| 2-Methyl-6-o.-tolylethynyl-pyridine | yellowish oil |
| 2-(3,4-Difluoro-phenylethynyl)-6-methyl-pyridine | 65-68 |
| 2-Methyl-6-[2-(2,3,5-trichloro-phenyl)-vinyl]-pyridine | 80-82 |
| 1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-ethanone | 76-78 |
| 2-Methyl-6-(3-trifluoromethyl-phenylethynyl)-pyridine | 35-37 |
| 2-Methyl-6-(3-nitro-phenylethynyl)-pyridine | 99.5-102.5 |
| 6-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-2-methyl-pyridine | 98-100 |
| {2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-morpholin-4-yl-methanone | 123-125 |
| (3-[2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy]-propyl)-dimethyl-amine hydrochloride salt | 207-210 |
| N-[4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl]-succinamic acid | 201 dec |
| N-[4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl]-2-phenyl-acetamide | 236-237 dec |
| ((4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl)-methyl)-carbamic acid .tert.-butyl ester | 144-145 dec |
| 1-tert.-Butyl-3-[4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl]-urea | 209 dec |
| {3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine hydrochloride salt | 161-162 |
| Cyclohexylmethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine hydrochloride salt | 178-179 dec |
| {4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine | 100 |
| Cyclohexylmethyl-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine | 106-107 |
| 2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-3-phenyl-propionamide | 102 |
| 2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide | 105 |
| 2-Amino-N-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide | 217-219 dec |
| 1-[1-({2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetyl)-piperidin-4-yl]-imidazolidin-2-one | amorphous foam |
| (1-[4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino]-ethyl)-phosphonic acid dimethyl ester | orange amorphous solid |
| 2-[2-(2-Methoxy-phenyl)-vinyl]-6-methyl-pyridine | 129-130 |

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| 2-(3-Ethoxy-4-fluoro-phenylethynyl)-6-methyl-pyridine | 82-83 |
| 2-(3-Chloro-phenylethynyl)-6-methyl-pyridine | 57-59 |
| 1-(3-Pyridin-2-ylethynyl-phenyl)-ethanone | 48-51 |
| 4-Chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 256-260 |
| 4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 121-123 |
| 2-Methyl-6-m-tolylethynyl-pyridine | 57-58 |
| 2-(2,5-Difluoro-phenylethynyl)-6-methyl-pyridine | 49-50 |
| 2-(3,5-Dimethyl-phenylethynyl)-6-methyl-pyridine | yellowish oil |
| 2-[2-(3,5-Dibromo-phenyl)-vinyl]-6-methyl-pyridine | 68-70 |
| 2-Methyl-6-[2-(pyrimidin-5-yl)-ethynyl]-pyridine | 110-112 |
| (2-[2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy]-ethyl)-dimethyl-amine | 165-167 |
| Acetic acid 1-[4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl]-ethyl ester | |
| 3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol | 250-251 |
| 3-(6-Methyl-pyridin-2-ylethynyl)-phenylamine | 129-130 |
| N-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-2-phenyl-acetamide | 133-135 dec |
| Thiophene-2-carboxylic acid [3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-amide | 156-157 dec |
| 2-Methyl-6-(thiophen-2-ylethynyl)-pyridine | 34-36 |
| 3-(6-Methyl-pyridin-2-ylethynyl)-benzoic acid ethyl ester | 56-58 |
| 2-(3,5-Dibromo-phenylethynyl)-6-methyl-pyridine | 100:101 |
| {2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ylmethyl}-dimethyl-amine | 227-229 dec |
| (3-[6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yloxy]-propyl)-dimethyl- | 184-186 |
| 5-Azido-4-iodo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | red glass |
| 2,6-Di-tert-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 126-127 |
| 1-[4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl]-ethanol | 97-99 |
| 2-Methyl-6-[2-(pyrimidin-2-yl)-ethynyl]-pyridine | 144-145 |
| [3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-phenyl-methanone | 99-100 |
| 6-(6-Methyl-pyridin-2-ylethynyl)-3,4-dihydro-1H-quinolin-2-one | 189-191 |
| 2-(3-[2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy]-propyl)-isoindole-1,3-dione | 101-103 |
| 3-Methoxy-6-methyl-2-m-tolylethynyl-pyridine | brown oil |
| Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-4-nitro-phenyl ester | 129-131 |
| 6-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one | 160-165 |
| 2-Methyl-6-[2-(pyrazin-2-yl)-ethynyl]-pyridine | 95-96 |

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| N-Methyl-N-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-acetamide | 62-70 |
| 2-[2-(3,5-Bis-trifluoromethyl-phenyl)-1-ethoxy-vinyl]-6-methyl-pyridine | yellow oil |
| Acetic acid 2-phenylethynyl-pyridin-3-yl ester | brown oil |
| Acetic acid 6-methyl-2-m-tolylethynyl-pyridin-3-yl ester | brown oil |
| Acetic acid 4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenyl ester | 91-93 |
| 2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-4-nitro-phenol | 275 dec |
| Dimethyl-[3-(2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine | yellowish oil |
| Dimethyl-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-amine | 240-243 |
| 1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanone | 56-58 |
| 2-(3-Fluoro-phenylethynyl)-quinoline | 81-83 |
| Acetic acid 2-methyl-6-styryl-pyridin-3-yl ester | 93-96 |
| 4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol | 141-143 |
| 3-Ethoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol | 175-178 dec |
| 4-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol | 184-187 dec |
| Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-6-nitro-phenyl ester | 105-110 dec |
| Dimethyl-[3-(6-methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine | yellow gum |
| 2-Azido-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol | 155-157 dec |
| Dimethyl-[3-(6-methyl-2-m-tolylethynyl-pyridin-3-yloxy)-propyl]-amine | yellowish oil |
| 2-(3-Methanesulfonyl-phenylethynyl)-6-methyl-pyridine | 108-110 dec |
| 3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propylamine | 186-189 |
| 4-Azido-N-(3-{2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-2-hydroxy-benzamide | 99-102 dec |
| 3-[3-(3-Dimethylamino-propoxy)-6-methyl-pyridin-2-ylethynyl]-benzonitrile | yellow gum |
| 5-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one | 133-134 |
| 2-Methyl-6-(2,3,5-trichloro-phenylethynyl)-pyridine | 112-114 |
| 2-[2-(6-methyl-pyridin-3-yl)ethynyl]-6-methyl-pyridine | 118-119 |
| Dimethyl-[3-[6-methyl-2-(3-trifluoromethyl-phenylethynyl)-pyridin-3-yloxy]-propyl]-amine | yellow gum |
| 2-[2-(6-methyl-pyridin-3-yl)ethynyl]-3-methoxy 6-methyl-pyridine hydrochloride salt | 198-199 |
| 2-Methyl-6-(5,6,7,8-tetrahydro-naphthalen-2-ylethynyl)-pyridine | 50-51 |
| 3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine | 151-153 |
| (3-{4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-dimethyl-amine; | 211-215 |

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| [6-(3-Fluoro-phenylethynyl)-pyridin-2-yl]-dimethyl-amine | brown oil |
| 6'-(3-Fluoro-phenylethynyl)-3,4,5,6-tetrahydro-2.H.-[1,2]bipyridinyl | brown gum |
| {3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine | 158-160 |
| 4-Azido-.N.-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-benzamide | 161-163 dec |
| 1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid ethyl ester | 105-110 dec |
| 1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-3-ol | 108-109 |
| 2-Ethynyl-6-(3-fluoro-phenylethynyl)-pyridine | 89-90 |
| 3-Methyl-6-(6-methyl-pyridin-2-ylethynyl)-3H-benzooxazol-2-one | 172-174 |
| 1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid dimethylamide | 154-157 |
| 1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-4-ol | amorphous white solid |
| 5-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol | 150-151 dec |
| 5-[2-Bromo-2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol | 158-159 |
| 5-[2-(6-Methyl-pyridin-2-yl)-E-vinyl]-2-nitro-phenol | 171-173 |
| 5-[2-(6-Methyl-pyridin-2-yl)-Z-vinyl]-2-nitro-phenol | 108-110 |
| 4-Azido-2-hydroxy-.N.-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide | 180-182 dec |
| 5-(3-Dimethylamino-propoxy)-6-phenylethynyl-pyridine-2-carboxylic acid ethyl ester | 160-162 |
| 6-Methyl-2-styryl-pyrimidin-4-ol | 221-225 |
| 2-Ethyl-6-(3-fluoro-phenylethynyl)-pyridine | brown oil |
| 2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridine | 74-76 |
| 2-Methyl-6-(3-trifluoromethoxy-phenylethynyl)-pyridine | <30; brown crystals |
| 2-Methyl-6-(3-[1,2,4]triazol-1-yl-phenylethynyl)-pyridine | 128-130 |
| 4-(6-Methyl-pyridin-2-ylethynyl)-phthalonitrile | 138-140 |
| 2-Methyl-6-{2-[3-(1.H.-tetrazol-5-yl)-phenyl]-vinyl}-pyridine; compound with formic acid | 234-240 |
| 3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine | 97-100 |
| {3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine | 171-173 |
| 2-(3,5-Dimethyl-phenylethynyl)-3-methoxy-6-methyl-pyridine | yellowish oil |
| 2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-ol | 251-253 Dec. |

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| 6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid ethyl ester | 84-86 |
| 2-Azido-5-(6-methyl-pyridin-2-ylethynyl)-phenol | 153-155 dec |
| 6-(3,4-Dimethoxy-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester | 149-152 |
| 2-(4-Methoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine | 56-87 |
| 2-(3-Fluoro-phenylethynyl)-6-methoxy-pyridine | brown oil |
| 2-(3-Fluoro-phenylethynyl)-5-methyl-pyridine | 74-76 |
| 6-(3,5-Dichloro-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester | 195-198 |
| 5-(3-Dimethylamino-propoxy)-6-(3,5-dimethyl-phenylethynyl)-pyridine-2-carboxylic acid ethyl ester | 187-190 |
| 6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid | 173-175 |
| [6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanol | 116-118 |
| [4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone | 138-140 |
| 2-(3-Fluoro-phenylethynyl)-6-methyl-nicotinic acid ethyl ester | brown oil |
| 2-(3-Fluoro-phenylethynyl)-4,6-dimethyl-pyridine | brown oil |
| 6-(3-Fluoro-phenylethynyl)-.N.-(5-methoxy-indan-2-ylmethyl)-2-methyl-nicotinamide | 157-159 |
| {[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-amino}-phenyl-acetic acid methyl ester | 133-135 |
| 2-Methyl-6-(5-methyl-thiophen-2-ylethynyl)-pyridine | 58-59 |
| 2-Methyl-6-(2,3,5-trimethyl-phenylethynyl)-pyridine | brown oil |
| 3-{2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propan-1-ol | 86-88 |
| [6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-ylmethyl]-dimethyl-amine | 220-222 |
| 2,2-Dimethyl-propionic acid 3-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl ester | yellowish oil |
| 2-Azido-4-iodo-5-(6-methyl-pyridin-2-ylethynyl)-phenol | 140 dec |
| 6-Azido-2,4-diiodo-3-(6-methyl-pyridin-2-ylethynyl)-phenol | 162 dec |
| 4-Azido-2-hydroxy-5-iodo-.N.-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide | 185 dec |
| Acetic acid 3-acetoxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-benzyl ester | brown oil |
| (Benzyl-[[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-acetyl]-amino)-acetic acid ethyl ester | brown oil |
| 2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid ethyl ester | 76-77 |

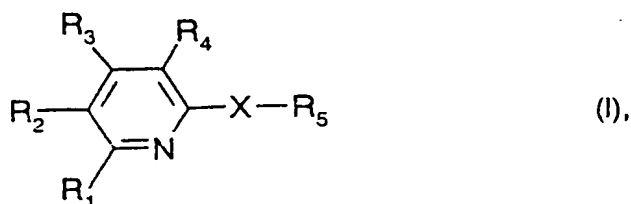
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| 3-[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propan-1-ol | 72-74 |
| [3-Hydroxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-phenyl]-methanol | 115-117 |
| (3-{2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine | yellowish gum |
| [4-(4-Fluoro-benzoyl)-piperidin-1-yl]-{6-[2-(3-fluoro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-methanone | 156-158 |
| 2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid | 245-248 |
| {6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-[4-(4-fluoro-benzoyl)-piperidin-1-yl]-methanone | 109-112 |
| 2-(3-Ethynyl-phenylethynyl)-6-methyl-pyridine | 48-49 |
| (3-{2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 207-210 |
| (3-{2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 161-169 |
| 4-[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazine-1-carboxylic acid .tert.-butyl ester | 97-99 |
| [6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-piperazin-1-yl-methanone | 250-252 dec |
| [4-(4-Azido-2-hydroxy-benzoyl)-piperazin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone | 186-188 dec |
| (3-{2-[2-(2,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 170-176 |
| 2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid ethyl ester | 89-91 |
| 2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid .tert.-butyl ester | 94-96 |
| 2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid | 231 dec |
| [2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanol | 143-146 |
| [4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanone | 156-158 |
| 3-Allyloxy-2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridine | 105-106 |
| [2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-morpholin-4-yl-methanone | 114-116 |
| Acetic acid 3-(6-methyl-pyridin-2-ylethynyl)-benzyl ester | brown oil |
| [2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-ylmethyl]-dimethyl-amine | 209-212 |
| (3-{2-[2-(3,5-Dichloro-phenyl)-propenyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 182-184 |
| 2-(3-Fluoro-phenylethynyl)-3-methoxy-6-methyl-pyridine | yellowish oil |

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| (3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 171-174 |
| (4-Azido-2-hydroxy-5-iodo-phenyl)-{4-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazin-1-yl}-methanone | 195-200 dec |
| 4-Azido-.N.-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-5-iodo-benzamide | 142-150 dec |
| 4-(2-Pyridin-2-yl-vinyl)-benzoic acid ethyl ester | 100-102 |
| (3-{2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 159-171 |
| [3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-methanol | 43-45 |
| 6-(3-Fluoro-phenylethynyl)-nicotinic acid .tert.-butyl ester | 96-98 |
| (3-{2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine hydrochloride salt | 174-177 |
| 2-(1-Bromo-2-phenyl-vinyl)-4-methyl-pyrimidine | yellow oil |
| 6-(3-Fluoro-phenylethynyl)-nicotinic acid | 223 dec. |
| [4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-pyridin-3-yl]-methanone | 136.0-139.0 |
| 2-(2-.tert.-Butoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine | 72.0-74.0 |
| 2-Methyl-6-[2-(2,4,5-trifluoro-phenyl)-vinyl]-pyridine | 74-76 |
| 2-Methyl-6-[2-(2,3,4-trifluoro-phenyl)-vinyl]-pyridine | 79-82 |
| 3-(6-Methyl-pyridin-2-ylethynyl)-phenol | 142-144 |
| 2-Methyl-6-[2-(3,4,5-trifluoro-phenyl)-vinyl]-pyridine | 74-76 |
| 2-(3-Methoxy-phenylethynyl)-6-methyl-pyridine | 55-57 |
| 2-Methyl-6-(2,3,4-trifluoro-phenylethynyl)-pyridine | 104-106 |

(dec = decomposition)

Claims:

1. A 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo- pyridine or a pharmaceutically acceptable salt thereof, for use in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.
2. A 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-arylazo- and 2-heteroarylazo- pyridine or a pharmaceutically acceptable salt thereof, for use in the treatment of epilepsy, cerebral ischemia, ischemic diseases of the eye, muscle spasms, convulsions, pain, acute, traumatic and chronic degenerative processes of the nervous system and psychiatric diseases.
3. A compound of formula I



wherein

R₁ denotes hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkyl-amino, piperidino, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower-alkyl-N-phenylcarbamoyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy,

R₂ denotes hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t-butylloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R₃ represents hydrogen, lower alkyl; carboxy, lower alkoxy-carbonyl, lower alkyl-carbamoyl, hydroxy-lower alkyl, di-lower alkyl-aminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R₄ represents hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy,

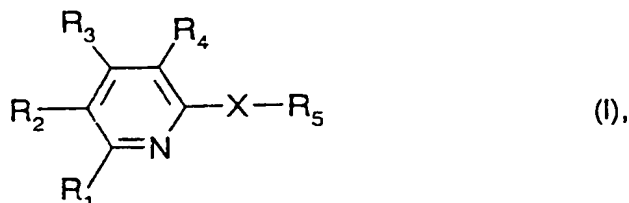
phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower-alkoxy or esterified carboxy-lower-alkoxy, X represents an optionally halo-substituted lower alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms or an azo (-N=N-) group, and R₅ denotes an aromatic or heteroaromatic group which is unsubstituted or substituted by one or more substituents selected from lower alkyl, halo, halo-lower alkyl, halo-lower alkoxy, lower alkenyl, lower alkynyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkynyl, hydroxy, hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, amino-, lower alkylamino-, lower alkanoylamino- or N-lower alkyl-N-lower alkanoylamino-lower alkoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, carboxy-lower alkylamino, esterified carboxy-lower alkylamino, amidated carboxy-lower alkylamino, phosphono-lower alkylamino, esterified phosphono-lower alkylamino, nitro, amino, lower alkylamino, di-lower alkylamino, acylamino, N-acyl-N-lower alkylamino, phenylamino, phenyl-lower alkylamino, cycloalkyl-lower alkylamino or heteroaryl-lower alkylamino each of which may be unsubstituted or lower alkyl-lower alkoxy-, halo- and/or trifluoromethyl-substituted, in free form or in form of a photoaffinity ligand, a radioactive marker, an N-oxide or a pharmaceutically acceptable salt,

for use in the treatment of disorders associated with irregularities of the glutaminergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

4. The use of a compound according to claim 3, in the treatment of disorders associated with irregularities of the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.
5. The use of a compound according to claim 3, for the manufacture of a pharmaceutical composition designed for the treatment of disorders associated with irregularities of

the glutamatergic signal transmission, and of nervous system disorders mediated full or in part by mGluR5.

6. A compound of formula I



wherein

R₁ denotes hydrogen, lower alkyl, hydroxy-lower alkyl, lower alkyl-amino, piperidino, carboxy, esterified carboxy, amidated carboxy, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted N-lower-alkyl-N-phenylcarbonyl, lower alkoxy, halo-lower alkyl or halo-lower alkoxy,

R₂ denotes hydrogen, lower alkyl, carboxy, esterified carboxy, amidated carboxy, hydroxy-lower alkyl, hydroxy, lower alkoxy or lower alkanoyloxy, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t-butylloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R₃ represents hydrogen, lower alkyl, carboxy, lower alkoxy-carbonyl, lower alkyl-carbamoyl, hydroxy-lower alkyl, di-lower alkyl-aminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R₄ represents hydrogen, lower alkyl, hydroxy, hydroxy-lower alkyl, amino-lower alkyl, lower alkylamino-lower alkyl, di-lower alkylamino-lower alkyl, unsubstituted or hydroxy-substituted lower alkyleneamino-lower alkyl, lower alkoxy, lower alkanoyloxy, amino-lower alkoxy, lower alkylamino-lower alkoxy, di-lower alkylamino-lower alkoxy, phthalimido-lower alkoxy, unsubstituted or hydroxy- or 2-oxo-imidazolidin-1-yl-substituted lower alkyleneamino-lower alkoxy, carboxy, esterified or amidated carboxy, carboxy-lower-alkoxy or esterified carboxy-lower-alkoxy,

X represents an optionally halo-substituted lower alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms or an azo (-N=N-) group, and

R₅ denotes an aromatic or heteroaromatic group which is unsubstituted or substituted by one or more substituents selected from lower alkyl, halo, halo-lower alkyl, halo-lower alkoxy, lower alkenyl, lower alkynyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl, unsubstituted or lower alkyl-, lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkynyl, hydroxy,

hydroxy-lower alkyl, lower alkanoyloxy-lower alkyl, lower alkoxy, lower alkenyloxy, lower alkylenedioxy, lower alkanoyloxy, amino-, lower alkylamino-, lower alkanoylamino- or N-lower alkyl-N-lower alkanoylamino-lower alkoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenoxy, unsubstituted or lower alkyl- lower alkoxy-, halo- and/or trifluoromethyl-substituted phenyl-lower alkoxy, acyl, carboxy, esterified carboxy, amidated carboxy, cyano, carboxy-lower alkylamino, esterified carboxy-lower alkylamino, amidated carboxy-lower alkylamino, phosphono-lower alkylamino, esterified phosphono-lower alkylamino, nitro, amino, lower alkylamino, di-lower alkylamino, acylamino, N-acyl-N-lower alkylamino, phenylamino, phenyl-lower alkylamino, cycloalkyl-lower alkylamino or heteroaryl-lower alkylamino each of which may be unsubstituted or lower alkyl-lower alkoxy-, halo- and/or trifluoromethyl-substituted, in free form or in form of a photoaffinity ligand, a radioactive marker, an N-oxide or a pharmaceutically acceptable salt, provided that, when R₃ is hydrogen,

a) in compounds of the formula I in which R₁, R₂ and R₄ are hydrogen, R₅ is different from phenyl, monohalophenyl, 2,4- and 3,4-dichlorophenyl, 3- and 4-trifluoromethylphenyl, methylphenyl, 3,4- and 2,5-dimethylphenyl, 4-isopropylphenyl, 3,5-di-tert.-butylphenyl, methoxyphenyl, 3,4-dimethoxyphenyl, 2,4,5- and 3,4,5-trimethoxyphenyl, hydroxyphenyl, 3,5-dihydroxyphenyl, 4-hydroxy-3,5-dimethylphenyl, 3-hydroxy-4-methoxy- and 4-hydroxy-3-methoxy-phenyl, 4-hydroxy-(3-methyl-5-tert.-butyl-, 2- and 4-acetylaminophenyl, 3,5-diisopropyl- and 3,5-di-tert.-butyl)phenyl, 4-carboxy- and 4-ethoxycarbonylphenyl, 4-cyanophenyl, 3-methoxycarbonylphenyl, 3-carboxy-5-methoxy-phenyl, 2-pyridinyl, 5-chloro-2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene, or R₅ is different from phenyl, 4-methylphenyl, 4-methoxyphenyl, 4-bromophenyl and 2- and 4-chlorophenyl when X denotes 1,2-propylene attached to R₅ in 2-position, or R₅ is different from phenyl, 2- and 4-chlorophenyl and 3-methoxyphenyl when X denotes 1,2-propylene attached to R₅ in 1-position, or R₅ is different from 4-methoxyphenyl when X denotes 2,3-but-2-enylene or 1,2-but-1-enylene attached to R₅ in 2-position, or R₅ is different from 4-methoxyphenyl and 4-isopropylphenyl when X denotes 2,3-pent-2-enylene attached to R₅ in 3-position, or R₅ is different from phenyl, 4-methylphenyl, methoxyphenyl and 4-hydroxyphenyl when X denotes 3,4-hex-3-enylene;

b) in compounds of the formula I in which R₁ is methyl and R₂ and R₄ are hydrogen, R₅ is different from phenyl, 3-methylphenyl, 2-methoxyphenyl, 2-chlorophenyl, 4-cyanophenyl, 2-pyridinyl and 6-methyl-2-pyridinyl when X denotes ethenylene;

c) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is carboxy, R_5 is different from phenyl, 3-methylphenyl, 4-methoxyphenyl and 4-bromophenyl when X denotes ethenylene;

d) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is methyl, R_5 is different from phenyl, 3-methoxy-, 4-methoxy- and 3,4-dimethoxyphenyl, 2-chloro- and 2,4-dichlorophenyl and 6-methyl-pyrid-2-yl when X denotes ethenylene or R_5 is different from phenyl when X is 1,2-prop-1-enylene attached to R_5 in 2-position;

e) in compounds of the formula I wherein R_1 and R_2 are hydrogen and R_4 is 2-dimethylaminoethoxycarbonyl or 3-dimethylaminopropylloxycarbonyl, R_5 is different from 4-methoxyphenyl when X denotes ethenylene;

f) in compounds of the formula I in which R_1 and R_2 are hydrogen and R_4 is 2-dimethoxyethoxy, R_5 is different from phenyl, 4-methylphenyl and 4-methoxycarbonylphenyl when X denotes ethenylene;

g) R_5 is different from phenyl when R_1 and R_2 are hydrogen and R_4 is hydroxy or ethoxycarbonyl, or when R_1 and R_2 are hydrogen and R_4 is hydroxy, or when R_1 is methyl, R_2 is hydrogen and R_4 is methoxy, or R_1 is but-1-enyl, R_2 is hydrogen and R_4 is hydrogen, or R_1 is hydrogen and R_4 is 2-dimethoxyethoxy, and X is, in each case, ethenylene,

and provided that, when R_3 is hydrogen and X is ethynylene,

a') R_5 is different from phenyl, 2- and 4-nitrophenyl, 4-aminophenyl, 4-chlorophenyl, 4-methylphenyl, 4-methoxyphenyl, 4-ethoxycarbonylphenyl, 5-formyl-2-methoxy-phenyl, 5-carboxy-2-methoxy-phenyl and pyridyl when R_1 , R_2 and R_4 are hydrogen;

b') in compounds of the formula I in which R_2 and R_4 are hydrogen, R_5 is different from phenyl, 3-methylphenyl, 6-methylpyridin-2-yl and 2-methoxyphenyl when R_1 is methyl, R_5 is different from 6-bromopyridin-2-yl when R_1 is bromo, and R_5 is different from 6-hexyloxypyridin-2-yl when R_1 denotes hexyloxy;

c') in compounds of the formula I wherein R_1 and R_4 are hydrogen, R_5 is different from phenyl, 4-aminophenyl and 4-propylphenyl when R_2 is methyl, R_5 is different from phenyl, 4-cyanophenyl and 4-pentylphenyl when R_2 is ethyl, R_5 is different from 3-cyano-4-ethoxy-phenyl and 3-bromo-4-methoxy-phenyl when R_2 is butyl, R_5 is different from 4-methoxyphenyl and 4-butyloxyphenyl when R_2 is pentyl, R_5 is different from 4-tert.-butylphenyl, 3-tert.-butyl-4-hydroxy-phenyl, 4-tert.-butyl-3-hydroxy-phenyl, and 4-hexyloxyphenyl when R_2 is carboxy, R_5 is different from phenyl when R_2 is methoxycarbonyl or methylcarbonyl, R_4 is different from 3-tert.-butylphenyl, 3-tert.-butyl-4-hydroxy-phenyl and 4-(4-methylpentyl)phenyl when R_2 is ethoxycarbonyl, and R_5 is different from 4-pentyloxyphenyl when R_2 is 2-methylbutyloxycarbonyl;

d') in compounds of the formula I wherein R_1 and R_2 are hydrogen, R_5 is different from phenyl when R_4 is hydroxy, methyl, ethyl, carboxy, methoxycarbonyl or carbamoyl.

7. A compound according to claim 6, wherein

X represents an optionally halo-substituted (C₂₋₄)alkenylene or alkynylene group bonded via vicinal unsaturated carbon atoms,

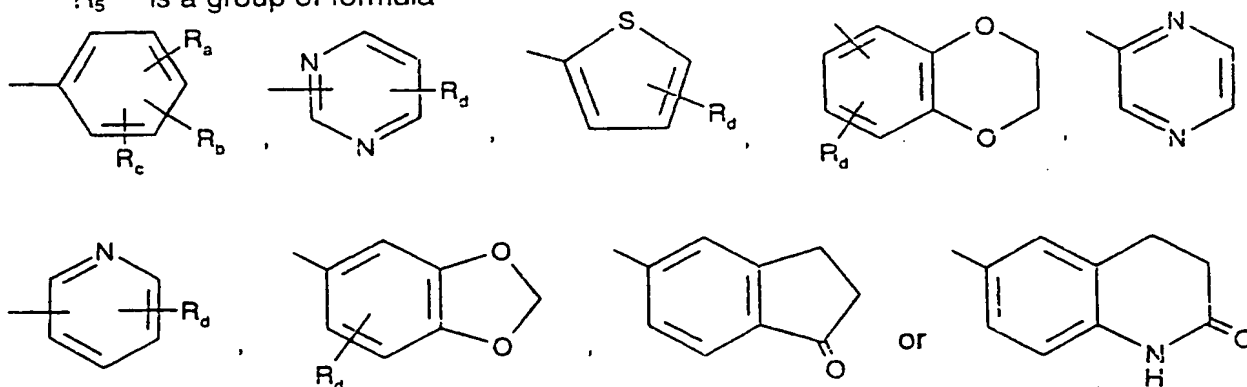
R_1 is hydrogen, (C₁₋₄) alkyl, (C₁₋₄)alkoxy, hydroxy(C₁₋₄)alkyl, cyano, ethynyl, carboxy, (C₁₋₄)alkoxycarbonyl, di(C₁₋₄)alkylamino, (C₁₋₆)alkylaminocarbonyl, trifluoromethylphenylaminocarbonyl,

R_2 is hydrogen, hydroxy, (C₁₋₄) alkyl, hydroxy (C₁₋₄) alkyl, (C₁₋₄) alkoxy, carboxy, (C₂₋₅)alkanoyloxy, (C₁₋₄) alkoxycarbonyl, di(C₁₋₄)alkylamino(C₁₋₄)alkanoyl, di(C₁₋₄)alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t-butylloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R_3 is hydrogen, (C₁₋₄) alkyl, carboxy, (C₁₋₄)alkoxycarbonyl, (C₁₋₄)alkylcarbamoyl, hydroxy(C₁₋₄)alkyl, di(C₁₋₄)alkylaminomethyl, morpholinocarbonyl or 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy,

R_4 is hydrogen, hydroxy, (C₁₋₄)alkoxy, carboxy, (C₂₋₅)alkanoyloxy, (C₁₋₄)alkoxycarbonyl, amino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkyl, carboxy (C₁₋₄)alkylcarbonyl, (C₁₋₄)alkoxycarbonyl-(C₁₋₄)alkoxy, hydroxy(C₁₋₄)alkyl, di(C₁₋₄)alkylamino(C₁₋₄)alkoxy, m-hydroxy-p-azidophenylcarbonylamino(C₁₋₄)alkoxy, and

R_5 is a group of formula



wherein

R_a and R_b independently are hydrogen, hydroxy, halogen, nitro, cyano, carboxy, (C₁₋₄)alkyl, (C₁₋₄)alkoxy, hydroxy(C₁₋₄)alkyl, (C₁₋₄)alkoxycarbonyl, (C₂₋₇)alkanoyl,

(C₂₋₅)alkanoyloxy, (C₂₋₅)alkanoyloxy(C₁₋₄)alkyl, trifluoromethyl, trifluoromethoxy, trimethylsilylethynyl, (C₂₋₅)alkynyl, amino, azido, amino (C₁₋₄)alkoxy, (C₂₋₅)alkanoylamino(C₁₋₄)alkoxy, (C₁₋₄)alkylamino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkoxy, (C₁₋₄)alkylamino, di(C₁₋₄)alkylamino, monohalobenzylamino, thienylmethylamino, thienylcarbonylamino, trifluoromethylphenylaminocarbonyl, tetrazolyl, (C₂₋₅)alkanoylamino, benzylcarbonylamino, (C₁₋₄)alkylamino-carbonylamino, (C₁₋₄)alkoxycarbonyl-aminocarbonylamino or (C₁₋₄)alkylsulfonyl, R_c is hydrogen, fluorine, chlorine, bromine, hydroxy, (C₁₋₄)alkyl, (C₂₋₅)alkanoyloxy, (C₁₋₄)alkoxy or cyano, and R_d is hydrogen, halogen or (C₁₋₄)alkyl.

8. A compound according to claim 6, wherein

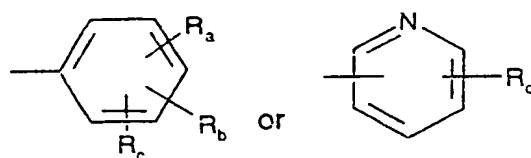
R₁ is hydrogen, (C₁₋₄) alkyl, (C₁₋₄)alkoxy, cyano, ethynyl or di(C₁₋₄)alkylamino,

R₂ is hydrogen, hydroxy, carboxy, (C₁₋₄) alkoxycarbonyl, di(C₁₋₄)alkylaminomethyl, 4-(4-fluoro-benzoyl)-piperidin-1-yl-carboxy, 4-t.-butyloxycarbonyl-piperazin-1-yl-carboxy, 4-(4-azido-2-hydroxybenzoyl)-piperazin-1-yl-carboxy or 4-(4-azido-2-hydroxy-3-iodo-benzoyl)-piperazin-1-yl-carboxy,

R₃ is as defined in claim 7,

R₄ is hydrogen, hydroxy, carboxy, (C₂₋₅)alkanoyloxy, (C₁₋₄)alkoxycarbonyl, amino (C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkoxy, di(C₁₋₄)alkylamino(C₁₋₄)alkyl or hydroxy(C₁₋₄)alkyl, and

R₅ is a group of formula



wherein

R_a and R_b independently are hydrogen, halogen, nitro, cyano,

(C₁₋₄)alkyl, (C₁₋₄)alkoxy, trifluoromethyl, trifluoromethoxy or (C₂₋₅)alkynyl, and

R_c and R_d are as defined in claim 7.

9. A compound according to claim 6, selected from

3-[2-(6-Methylpyridin-2-yl)-vinyl]-benzonitrile

2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile

2-Methyl-6-[2-(pyridin-4-yl)-vinyl]-pyridine
2-Methyl-6-[2-(pyridin-3-yl)-vinyl]-pyridine
2-[2-(3-Bromophenyl)ethynyl]-6-methyl-pyridine
3-[2-(6-Methylpyridin-2-yl)ethynyl]-benzonitrile
2-Styryl-pyridin-3-ol
2-Methyl-6-[2-(3-nitro-phenyl)-vinyl]-pyridine
Acetic acid 6-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester
6-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol
Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-pyridin-3-yl ester
2-[2-(2-Chloro-phenyl)-vinyl]-pyridin-3-ol
6-Methyl-2-styryl-pyridin-3-ol
Acetic acid 2-[2-(2-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
(Z)-6-Methyl-2-styryl-pyridin-3-ol
2-[2-(2-Nitro-phenyl)-vinyl]-pyridine
Acetic acid 2-[2-(4-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
Acetic acid 6-[2-(4-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester
2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
6-[2-(4-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol
Acetic acid 6-methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester
6-Methyl-2-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol
Acetic acid 2-methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-yl ester
2-Methyl-6-[2-(2-nitro-phenyl)-vinyl]-pyridin-3-ol
Acetic acid 2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
Acetic acid 6-[2-(3-chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester
2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol
(Z)-(6-Styryl-pyridin-2-yl)-methanol
(E)-(6-Styryl-pyridin-2-yl)-methanol
Dimethyl-[3-(6-methyl-2-styryl-pyridin-3-yloxy)-propyl]-amine;
2-Methyl-6-styryl-pyridine 1-oxide
2-Styryl-pyridine 1-oxide
(E)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol
(Z)-6-Methyl-2-(2-pyridin-2-yl-vinyl)-pyridin-3-ol;
6-Styryl-pyridine-2-carbonitrile
2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridine

3-Methoxy-6-methyl-2-styryl-pyridine
6-Styryl-pyridine-2-carboxylic acid amide
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzonitrile
6-Styryl-pyridine-2-carboxylic acid;
6-Styryl-pyridine-2-carboxylic acid methyl ester
Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol
Acetic acid 2-methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(2-Chloro-phenyl)-vinyl]-5-ethyl-pyridine
1-(6-Styryl-pyridin-2-yl)-ethanone
6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid ethyl ester
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid ethyl ester
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid;
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-benzoic acid methyl ester
2-Methoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-methanol;
6-Styryl-pyridine-2-carboxylic acid .tert.-butylamide
2-(2-Bromo-2-phenyl-vinyl)-6-methyl-pyridine;
6-Styryl-pyridine-2-carboxylic acid hexylamide;
6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-nicotinic acid
2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-nicotinic acid
2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridine
2-Methyl-6-[2-(3-trifluoromethyl-phenyl)-vinyl]-pyridine
(E)-6-[2-(4-Pyridyl)vinyl]-2-picoline
N,N-Diethyl-3-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide;
N,N-Diethyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-benzamide;
(E)-6-[2-(3-pyridyl)vinyl]-2-Picoline
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetic acid ethyl ester
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide;
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-.N.-(3-trifluoromethyl-phenyl)-benzamide
2-[2-(3-Nitro-phenyl)-vinyl]-pyridine

6-Styryl-pyridine-2-carboxylic acid (3-trifluoromethyl-phenyl)-amide
2-(6-Styryl-pyridin-2-yl)-propan-2-ol
2-Methyl-6-(2-thiophen-2-yl-vinyl)-pyridine
2-[2-(3-Cyano-phenyl)-vinyl]-pyridine
2-[2-(3-Bromo-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3-Bromo-phenyl)-2-fluoro-vinyl]-6-methyl-pyridine
2-[2-(3,5-Dimethylphenyl)-2-fluoro-vinyl]-6-methyl-pyridine
2-[2-(2,3-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3-Chloro-phenyl)-1-methyl-vinyl]-pyridine
[2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl]-methanol
2-Methyl-6-[2-(3-trimethylsilanylethynyl-phenyl)-vinyl]-pyridine
2-[2-(3,4-Difluoro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3-Ethynyl-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3-Methoxy-phenyl)-vinyl]-6-methyl-pyridine
2-Methyl-6-[2-(3-phenoxy-phenyl)-vinyl]-pyridine
2-[2-(3-Benzoyloxy-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(2,5-Difluoro-phenyl)-vinyl]-6-methyl-pyridine
[2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy]-acetic acid
(3-[2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy]-propyl)-dimethyl-amine
[6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl]-methanol
2-(3-Bromo-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-[2-[3-(3-trifluoromethyl-phenoxy)-phenyl]-vinyl]-pyridine
2-[2-(3,5-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3-Chloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine
Acetic acid 4-bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
Acetic acid 3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridine
4-Bromo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl ester
Acetic acid 6-[2-(3,5-dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl ester
Acetic acid 2-[2-(3,5-dichloro-phenyl)-vinyl]-pyridin-3-yl ester
2-Methyl-6-(2-naphthalen-1-yl-vinyl)-pyridine
2-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-vinyl]-6-methyl-pyridine

2-Methyl-6-(2-naphthalen-2-yl-vinyl)-pyridine
2-{2-[3-(3,5-Dichloro-phenoxy)-phenyl]-vinyl}-6-methyl-pyridine
2-[2-(3-Chloro-phenyl)-propenyl]-6-methyl-pyridine
2-[2-(2,3-Dihydro-benzofuran-5-yl)-vinyl]-6-methyl-pyridine
2-[2-(4-Fluoro-phenyl)-vinyl]-6-methyl-pyridine
2-Methyl-6-(2-o-tolyl-vinyl)-pyridine
2-Methyl-6-(2-p-tolyl-vinyl)-pyridine
2-Methyl-6-(2-p-tolyl-propenyl)-pyridine
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine
(2,3-Dimethoxy-7-nitro-quinoxalin-5-ylmethyl)-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-
amine
N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide
N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide
2,2-Dimethyl-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-propionamide
Thiophene-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide
Cyclohexanecarboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide
1-(4-Bromo-phenyl)-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea
2-Methyl-6-[2-(4-nitro-phenyl)-vinyl]-pyridine
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamine
2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
6-[2-(3,5-Dichloro-phenyl)-vinyl]-2-methyl-pyridin-3-ol
2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-ol
2-[2-(6-Chloro-benzo[1,3]dioxol-5-yl)-vinyl]-6-methyl-pyridine
2-[2-(2,3-Difluoro-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3,4-Dichloro-phenyl)-propenyl]-6-methyl-pyridine
2-[2-(3,5-Bis-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine
Acetic acid 2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
2-Methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
2-Methyl-6-[2-(2,3,6-trifluoro-phenyl)-vinyl]-pyridine
2-[2-(4-Fluoro-3-trifluoromethyl-phenyl)-vinyl]-6-methyl-pyridine
2-Methyl-6-(2,3,6-trifluoro-phenylethynyl)-pyridine
Acetic acid 4-chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
Acetic acid 2,6-di-tert.-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
3-(6-Methyl-pyridin-2-ylethynyl)-benzamide
Acetic acid 4-bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl ester
2-(6-Chloro-benzo[1,3]dioxol-5-ylethynyl)-6-methyl-pyridine

2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-6-methyl-pyridine
2-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-pyridine
5-Azido-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
2-[2-(Pyridin-3-yl)ethynyl]-6-methyl-pyridine
N-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid
1-tert.-Butyl-3-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea
5-({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino)-methyl)-7-nitro-1,4-dihydro-quinoxaline-2,3-dione
Tetrahydro-furan-2-carboxylic acid {3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amide
(1-{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-2-phenyl-ethyl)-carbamic acid tert.-butyl ester
(({3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-methyl)-carbamic acid tert.-butyl ester
Diethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine
Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine
Ethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine
2-(2-Ethoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine
2-(3,5-Difluoro-phenylethynyl)-6-methyl-pyridine
2-(3-Fluoro-phenylethynyl)-6-methyl-pyridine
2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridine
2-[2-(3,4-Dimethoxy-phenyl)-vinyl]-6-methyl-pyridine
2-(3,4-Dichloro-phenylethynyl)-6-methyl-pyridine
2-(4-Ethoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine
2-(4-Fluoro-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-o-tolylethynyl-pyridine
2-(3,4-Difluoro-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-[2-(2,3,5-trichloro-phenyl)-vinyl]-pyridine
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-ethanone
2-Methyl-6-(3-trifluoromethyl-phenylethynyl)-pyridine
2-Methyl-6-(3-nitro-phenylethynyl)-pyridine
6-[2-(3,5-Dichloro-phenyl)-vinyl]-3-methoxy-2-methyl-pyridine
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yl}-morpholin-4-yl-methanone
(3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
N-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-succinamic acid
N-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-2-phenyl-acetamide
(({4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylcarbamoyl}-methyl)-carbamic acid .tert.-butyl ester
1-(tert.-Butyl-3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-urea

{3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine hydrochloride salt
Cyclohexylmethyl-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine hydrochloride salt
{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-thiophen-2-ylmethyl-amine
Cyclohexylmethyl-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-amine
2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-3-phenyl-propionamide
2-Amino-N-{3-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide
2-Amino-N-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-acetamide
1-[1-({2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-acetyl)-piperidin-4-yl]-
imidazolidin-2-one
(1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenylamino}-ethyl)-phosphonic acid dimethyl ester
2-(3-Ethoxy-4-fluoro-phenylethynyl)-6-methyl-pyridine
2-(3-Chloro-phenylethynyl)-6-methyl-pyridine
1-(3-Pyridin-2-ylethynyl-phenyl)-ethanone
4-Chloro-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
2-(2,5-Difluoro-phenylethynyl)-6-methyl-pyridine
2-(3,5-Dimethyl-phenylethynyl)-6-methyl-pyridine
2-[2-(3,5-Dibromo-phenyl)-vinyl]-6-methyl-pyridine
3-(6-Methyl-pyridin-2-ylethynyl)-benzonitrile
2-Methyl-6-[2-(pyrimidin-5-yl)-ethynyl]-pyridine
(2-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-ethyl)-dimethyl-amine
Acetic acid 1-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenyl}-ethyl ester
3-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenol
3-(6-Methyl-pyridin-2-ylethynyl)-phenylamine
.N.-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-2-phenyl-acetamide
Thiophene-2-carboxylic acid [3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-amide
2-Methyl-6-thiophen-2-ylethynyl-pyridine
3-(6-Methyl-pyridin-2-ylethynyl)-benzoic acid ethyl ester
2-(3,5-Dibromo-phenylethynyl)-6-methyl-pyridine
{2-[2-(2-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-ylmethyl}-dimethyl-amine
(3-{6-[2-(3-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yloxy}-propyl)-dimethyl-
5-Azido-4-iodo-2-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
2,6-Di-tert.-butyl-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanol
2-Methyl-6-[2-(pyrimidin-2-yl)-ethynyl]-pyridine
[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-phenyl-methanone

6-(6-Methyl-pyridin-2-ylethynyl)-3,4-dihydro-1H-quinolin-2-one
2-(3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-isoindole-1,3-dione
3-Methoxy-6-methyl-2-m-tolylethynyl-pyridine
Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-4-nitro-phenyl ester
6-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one
2-Methyl-6-[2-(pyrazin-2-yl)-ethynyl]-pyridine
N-Methyl-N-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-acetamide
2-[2-(3,5-Bis-trifluoromethyl-phenyl)-1-ethoxy-vinyl]-6-methyl-pyridine
Acetic acid 2-phenylethynyl-pyridin-3-yl ester
Acetic acid 6-methyl-2-m-tolylethynyl-pyridin-3-yl ester
Acetic acid 4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenyl ester
2-[2-(6-Methyl-pyridin-2-yl)-vinyl]-4-nitro-phenol
Dimethyl-[3-(2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine
Dimethyl-(3-{4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-amine
1-{4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-phenyl}-ethanone
2-(3-Fluoro-phenylethynyl)-quinoline
Acetic acid 2-methyl-6-styryl-pyridin-3-yl ester
4-[2-(6-Methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol
3-Ethoxy-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol
4-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol
Acetic acid 2-[2-(6-methyl-pyridin-2-yl)-vinyl]-6-nitro-phenyl ester
Dimethyl-[3-(6-methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-amine
2-Azido-4-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenol
Dimethyl-[3-(6-methyl-2-m-tolylethynyl-pyridin-3-yloxy)-propyl]-amine
2-(3-Methanesulfonyl-phenylethynyl)-6-methyl-pyridine
3-{2-[2-(3-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propylamine
4-Azido-N-(3-{2-[2-(3-chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-2-hydroxy-benzamide
3-[3-(3-Dimethylamino-propoxy)-6-methyl-pyridin-2-ylethynyl]-benzonitrile
5-(6-Methyl-pyridin-2-ylethynyl)-indan-1-one
2-Methyl-6-(2,3,5-trichloro-phenylethynyl)-pyridine
2-[2-(6-methyl-pyridin-3-yl)ethynyl]-6-methyl-pyridine
Dimethyl-[3-[6-methyl-2-(3-trifluoromethyl-phenylethynyl)-pyridin-3-yloxy]-propyl]-amine
2-[2-(6-methyl-pyridin-3-yl)ethynyl]-3-methoxy 6-methyl-pyridine hydrochloride salt
2-Methyl-6-(5,6,7,8-tetrahydro-naphthalen-2-ylethynyl)-pyridine
3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine

(3-{4-Bromo-2-methoxy-6-[2-(6-methyl-pyridin-2-yl)-vinyl]-phenoxy}-propyl)-dimethyl-amine;
[6-(3-Fluoro-phenylethynyl)-pyridin-2-yl]-dimethyl-amine
6'-(3-Fluoro-phenylethynyl)-3,4,5,6-tetrahydro-2H-[1,2]bipyridinyl
{3-[2-(3-Chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine
4-Azido-N-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-
benzamide
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid ethyl ester
1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-3-ol
2-Ethynyl-6-(3-fluoro-phenylethynyl)-pyridine
3-Methyl-6-(6-methyl-pyridin-2-ylethynyl)-3H-benzooxazol-2-one
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid
1-[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-1H-[1,2,4]triazole-3-carboxylic acid dimethylamide
1-[3-(6-Methyl-2-phenylethynyl-pyridin-3-yloxy)-propyl]-piperidin-4-ol
5-(6-Methyl-pyridin-2-ylethynyl)-2-nitro-phenol
5-[2-Bromo-2-(6-methyl-pyridin-2-yl)-vinyl]-2-nitro-phenol
5-[2-(6-Methyl-pyridin-2-yl)-E-vinyl]-2-nitro-phenol
5-[2-(6-Methyl-pyridin-2-yl)-Z-vinyl]-2-nitro-phenol
4-Azido-2-hydroxy-N-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide
5-(3-Dimethylamino-propoxy)-6-phenylethynyl-pyridine-2-carboxylic acid ethyl ester
6-Methyl-2-styryl-pyrimidin-4-ol
2-Ethyl-6-(3-fluoro-phenylethynyl)-pyridine
2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-(3-trifluoromethoxy-phenylethynyl)-pyridine
2-Methyl-6-(3-[1,2,4]triazol-1-yl-phenylethynyl)-pyridine
4-(6-Methyl-pyridin-2-ylethynyl)-phthalonitrile
2-Methyl-6-[2-[3-(1H-tetrazol-5-yl)-phenyl]-vinyl]-pyridine; compound with formic acid
3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propylamine
{3-[2-(3,5-Dichloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-dimethyl-amine
2-(3,5-Dimethyl-phenylethynyl)-3-methoxy-6-methyl-pyridine
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-ol
6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid ethyl ester
2-Azido-5-(6-methyl-pyridin-2-ylethynyl)-phenol
6-(3,4-Dimethoxy-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid
ethyl ester
2-(4-Methoxy-3-trifluoromethyl-phenylethynyl)-6-methyl-pyridine
2-(3-Fluoro-phenylethynyl)-6-methoxy-pyridine

2-(3-Fluoro-phenylethynyl)-5-methyl-pyridine
6-(3,5-Dichloro-phenylethynyl)-5-(3-dimethylamino-propoxy)-pyridine-2-carboxylic acid ethyl ester
5-(3-Dimethylamino-propoxy)-6-(3,5-dimethyl-phenylethynyl)-pyridine-2-carboxylic acid ethyl ester
6-(3-Fluoro-phenylethynyl)-2-methyl-nicotinic acid
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanol
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone
2-(3-Fluoro-phenylethynyl)-6-methyl-nicotinic acid ethyl ester
2-(3-Fluoro-phenylethynyl)-4,6-dimethyl-pyridine
6-(3-Fluoro-phenylethynyl)-N-(5-methoxy-indan-2-ylmethyl)-2-methyl-nicotinamide
{[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-amino}-phenyl-acetic acid methyl ester
2-Methyl-6-(5-methyl-thiophen-2-ylethynyl)-pyridine
2-Methyl-6-(2,3,5-trimethyl-phenylethynyl)-pyridine
3-{2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propan-1-ol
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-ylmethyl]-dimethyl-amine
2,2-Dimethyl-propionic acid 3-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl ester
2-Azido-4-iodo-5-(6-methyl-pyridin-2-ylethynyl)-phenol
6-Azido-2,4-diiodo-3-(6-methyl-pyridin-2-ylethynyl)-phenol
4-Azido-2-hydroxy-5-iodo-N-[3-(6-methyl-pyridin-2-ylethynyl)-phenyl]-benzamide
Acetic acid 3-acetoxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-benzyl ester
(Benzyl-[[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-acetyl]-amino)-acetic acid ethyl ester
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid ethyl ester
3-[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propan-1-ol
[3-Hydroxymethyl-5-(6-methyl-pyridin-2-ylethynyl)-phenyl]-methanol
(3-{2-[2-(3,5-Dimethyl-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-[2-(3-fluoro-phenyl)-vinyl]-2-methyl-pyridin-3-yl]-methanone
2-[2-(3-Fluoro-phenyl)-vinyl]-6-methyl-isonicotinic acid
{6-[2-(2-Chloro-phenyl)-vinyl]-2-methyl-pyridin-3-yl}-[4-(4-fluoro-benzoyl)-piperidin-1-yl]-methanone
2-(3-Ethynyl-phenylethynyl)-6-methyl-pyridine

(3-{2-[2-(2,6-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
(3-{2-[2-(2,3-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
4-[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazine-1-carboxylic acid
tert.-butyl ester
[6-(3-Fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-piperazin-1-yl-methanone
[4-(4-Azido-2-hydroxy-benzoyl)-piperazin-1-yl]-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridin-3-yl]-methanone
(3-{2-[2-(2,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid ethyl ester
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid .tert.-butyl ester
2-(3-Fluoro-phenylethynyl)-6-methyl-isonicotinic acid
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanol
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[2-(3-fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-methanone
3-Allyloxy-2-[2-(3,5-dichloro-phenyl)-vinyl]-6-methyl-pyridine
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-yl]-morpholin-4-yl-methanone
Acetic acid 3-(6-methyl-pyridin-2-ylethynyl)-benzyl ester
[2-(3-Fluoro-phenylethynyl)-6-methyl-pyridin-4-ylmethyl]-dimethyl-amine
(3-{2-[2-(3,5-Dichloro-phenyl)-propenyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
2-(3-Fluoro-phenylethynyl)-3-methoxy-6-methyl-pyridine
(3-{2-[2-(3,5-Dichloro-phenyl)-vinyl]-pyridin-3-yloxy}-propyl)-dimethyl-amine
(4-Azido-2-hydroxy-5-iodo-phenyl)-{4-[6-(3-fluoro-phenylethynyl)-2-methyl-pyridine-3-carbonyl]-piperazin-1-yl}-methanone
4-Azido-N-{3-[2-(3-chloro-phenylethynyl)-6-methyl-pyridin-3-yloxy]-propyl}-2-hydroxy-5-iodo-benzamide
4-(2-Pyridin-2-yl-vinyl)-benzoic acid ethyl ester
(3-{2-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
[3-(6-Methyl-pyridin-2-ylethynyl)-phenyl]-methanol
6-(3-Fluoro-phenylethynyl)-nicotinic acid tert.-butyl ester
(3-{2-[2-(3,4-Dichloro-phenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethyl-amine
2-(1-Bromo-2-phenyl-vinyl)-4-methyl-pyrimidine
6-(3-Fluoro-phenylethynyl)-nicotinic acid
[4-(4-Fluoro-benzoyl)-piperidin-1-yl]-[6-(3-fluoro-phenylethynyl)-pyridin-3-yl]-methanone
2-(2-tert.-Butoxy-3,6-difluoro-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-[2-(2,4,5-trifluoro-phenyl)-vinyl]-pyridine
2-Methyl-6-[2-(2,3,4-trifluoro-phenyl)-vinyl]-pyridine

3-(6-Methyl-pyridin-2-ylethynyl)-phenol
2-Methyl-6-[2-(3,4,5-trifluoro-phenyl)-vinyl]-pyridine
2-(3-Methoxy-phenylethynyl)-6-methyl-pyridine
2-Methyl-6-(2,3,4-trifluoro-phenylethynyl)-pyridine
and pharmaceutically acceptable salts thereof.

10. (3-{2-[2-trans-(3,5-dichlorophenyl)-vinyl]-6-methyl-pyridin-3-yloxy}-propyl)-dimethylamine in free form or in form of a pharmaceutically acceptable salt.
11. A pharmaceutical composition comprising as pharmaceutical active ingredient, together with customary pharmaceutical excipients, a compound according to any of claims 6 to 10, in free form or in form of a pharmaceutically acceptable salt.
12. A method of treating disorders mediated full or in part by mGluR1 or mGluR5, which method comprises administering to a warm-blooded organism in need of such treatment a therapeutically effective amount of an 2-arylalkenyl-, 2-heteroarylalkenyl-, 2-arylalkynyl-, 2-heteroarylalkynyl-, 2-aryloxy- and 2-heteroaryloxy- pyridine or a pharmaceutically acceptable salt thereof.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (51) International Patent Classification ⁶ : C07D 213/65, A61K 31/44, C07D 213/80, 401/12, 401/06 | | A3 | (11) International Publication Number: WO 99/02497 |
| | | | (43) International Publication Date: 21 January 1999 (21.01.99) |
| (21) International Application Number: PCT/EP98/04266 (22) International Filing Date: 9 July 1998 (09.07.98) (30) Priority Data: 08/891,691 11 July 1997 (11.07.97) US 08/890,689 11 July 1997 (11.07.97) US (71) Applicant (for all designated States except AT US): NOVARTIS AG [CH/CH]; Schwarzwaldallee 215, CH-4058 Basel (CH). (71) Applicant (for AT only): NOVARTIS-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT MBH [AT/AT]; Brunner Strasse 59, A-1235 Vienna (AT). (71) Applicant (for all designated States except US): SIBIA NEUROSCIENCES INC. [US/US]; Suite 300, 505 Coast Boulevard South, La Jolla, CA 92037-4641 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): ALLGEIER, Hans [DE/DE]; Lichsenweg 20, D-79541 Lörrach (DE). AUBERSON, Yves [CH/CH]; Kurzellängeweg 7 A, CH-4123 Allschwil (CH). BIOLLAZ, Michel [CH/CH]; Im Kugelfang 31, CH-4102 Binningen (CH). COSFORD, Nicholas, David [GB/US]; 7161 Rock Valley Court, San Diego, CA 92122 (US). GASPARINI, Fabrizio [CH/CH]; Weiherhofstrasse 10, CH-4415 Lausen (CH). HECK- | | ENDORN, Roland [CH/CH]; Blumenweg 20, CH-4144 Arlesheim (CH). JOHNSON, Edwin, Carl [US/US]; 13240 Gunner Drive, San Diego, CA 92129 (US). KUHN, Rainer [DE/DE]; Josef-Pfeffer-Weg 7, D-79540 Lörrach (DE). VARNEY, Mark, Andrew [GB/US]; 13202 Thunderhead Street, San Diego, CA 92129 (US). VELİÇELEBİ, Gönül [US/US]; 4688 Tarantella Lane, San Diego, CA 92130 (US). (74) Agent: BECKER, Konrad; Novartis AG, Patent- und Markenabteilung, Lichtstrasse 35, CH-4002 Basel (CH). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published With international search report. (88) Date of publication of the international search report: 1 April 1999 (01.04.99) | |
| (54) Title: PYRIDINE DERIVATIVES | | | |
| <div style="text-align: center;"> <p style="text-align: right;">(I)</p> </div> | | | |
| (57) Abstract | | | |
| Compounds of the formula (I), wherein X and R ₁ to R ₅ are as defined in the description, are useful for treating disorders mediated full or in part by mGluR5. | | | |

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/04266

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D213/65 A61K31/44 C07D213/80 C07D401/12 C07D401/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

9 December 1998

Date of mailing of the international search report

07.01.99

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Lauro, P

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/04266

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 98/04266

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 98/04266

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 4, 12
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 4 and 12 are directed to a method for treatment of the human/animal body by therapy, the search has been carried out and based on the alleged effects of the compounds/compositions
2. ☒ Claims Nos.: -
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

In view of the huge number of documents which disclose the compounds claimed in claims 1-3, 6-11, and which could not all be cited in the search report, the search is to be considered incomplete as far as the claims directed to compounds per se and their pharmaceutical compositions are concerned. The compounds in the form of photoaffinity ligands and radioactive markers have not been searched since no support in the description could be found. Claim 5 has been searched completely.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 98/04266

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